Health-Related Quality of Life and Tolerability in Patients With/Without Skin Toxicity During Loncastuximab Tesirine Treatment in a Phase 2 Clinical Trial (LOTIS-2)

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ABSTRACT

CONTEXT: Skin toxicity was commonly reported among patients treated with loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca). Most skin toxicities (~90%) were grade 1 or 2, but their impact on health-related quality of life (HRQOL) was unknown.

OBJECTIVE: This post hoc analysis assesses whether the skin toxicity is associated with HRQOL and patient tolerability to Lonca.

DESIGN: The LOTIS-2 study (NCT03589469) is a single-arm, open-label, phase 2 study of 145 adult patients with relapsed/refractory diffuse large B-cell lymphoma after ≥ 2 prior treatments. Patients received Lonca as an intravenous infusion on day 1 of each 3-week treatment cycle for up to 1 year. EQ-5D and FACT-Lym scores were collected. Mean changes from baseline were summarized by visit and with/without skin toxicity. The least squares means of the differences were estimated using the analysis of covariance models to adjust for age, sex, race, baseline score, and tumor response status. Treatment tolerability was measured using FACT-Lym item GP5 ("I am bothered by side effects of treatment").

RESULTS: Patients with a HRQOL baseline score and a postbaseline score (n = 130) were included in the analysis (median age, 66 years; 59% male; and 88% White). With the median 4 cycles of treatment (range, 1-26), 41% of patients experienced skin toxicity during treatment with > 80% due to nonphotosensitivity cutaneous reactions. Among all 9 evaluated scores (EQ-5D visual analog scale, FACT-Lym subscale and composite scores) for visits up to cycle 9 (n ≥ 20), there were no significant differences ($P > 0.05$) between patients with and without skin toxicity except for FACT-Lym total at cycle 9 (worse in patients with skin toxicity). A majority of patients (≥ 60%) were "not at all" or "a little bit" bothered in both groups at each cycle, although a higher percentage of patients with skin toxicity reported "a little bit" than those without skin toxicity after 2 cycles.

CONCLUSIONS: Patients with skin toxicity while receiving Lonca did not experience different HRQOL compared with patients without skin toxicity in most visits. Lonca was tolerated even among patients with skin toxicity. (Sponsored by ADC Therapeutics).

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 2 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 (R/R) DLBCL after ≥ 2 prior therapies.[1,2]
- Skin and subcutaneous tissue disorders were reported by nearly half of the patients treated with Lonca. Most of them (~90%) were grade 1 or 2, but their impact on HRQOL was unknown.

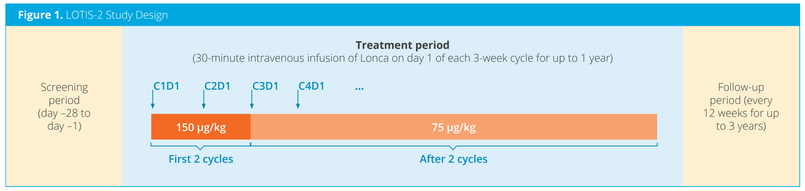
OBJECTIVE

- This post hoc analysis assesses whether the skin toxicity is associated with HRQOL and patient tolerability to Lonca.

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 2 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 group with skin toxicity consisted of patients who experienced photosensitivity and/or nonphotosensitivity cutaneous reactions during the treatment. The group without skin toxicity is the rest of the patients.

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.

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 (recall period: past 7 days) includes 5 subscale scores and 3 composite scores with higher scores indicating better HRQOL. The Lymphoma Subscale measures lymphoma-specific symptoms and concerns.
    - FACT-Lym total = FACT-G total + Lymphoma subscale
    - FACT-G total = Physical well-being + Social/family well-being + Emotional well-being + Functional well-being
    - Trial outcome index = Physical well-being + Functional well-being + Lymphoma subscale
  - 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 with/without skin toxicity.
- Analysis of covariance models were conducted for EQ-5D VAS and FACT-Lym subscale and composite scores to estimate the least squares mean changes from baseline in the group with or without skin toxicity, as well as the differences between the 2 groups. The models included skin toxicity group (with or without skin toxicity), age, sex, race, baseline score, and tumor response (best response of complete or partial response vs. other) as covariates.
- Percentages of responses to GP5 (tolerability) were summarized by visits and skin toxicity group.
- Analysis was conducted by 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.

RESULTS

- The LOTIS-2 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 treated with Lonca, and only 5 patients were still treated at cycle 15.
- Patients with a baseline score and at least 1 postbaseline score were included in the analysis (Table 1).
  - Of the 130 patients included, the median age was 66 years, 59% were male, and 88% were White.
  - Patients with skin toxicity were less heavily treated previously. They also responded better to Lonca.
- With the median 4 cycles of treatment (range, 1-26), 41% of patients experienced skin toxicity during treatment with > 80% due to nonphotosensitivity cutaneous reactions.
- Among all 9 evaluated scores (EQ-5D VAS, FACT-Lym subscale and composite scores) for visits up to cycle 9 (n ≥ 20), there were no significant differences ($P > 0.05$) between patients with and without skin toxicity except for FACT-Lym total at cycle 9 (worse in patients with skin toxicity).
- A majority of patients (≥ 60%) were "not at all" or "a little bit" bothered in both groups at each cycle, although a higher percentage of patients with skin toxicity reported "a little bit" than those without skin toxicity after 2 cycles.

Table 1. Baseline Characteristics and Tumor Response

	Without skin toxicity (N = 77)	With skin toxicity (N = 53)	Overall (N = 130)
Baseline characteristics			
Age, years, median (range)	65 (24-94)	67 (25-85)	66 (24-94)
Sex, male, n (%)	43 (56)	34 (64)	77 (59)
Race, White, n (%)	66 (86)	49 (93)	115 (88)
Prior systemic therapies, n (%)			
2 prior lines	28 (36)	31 (58)	59 (45)
3 prior lines	21 (27)	11 (21)	32 (25)
> 3 prior lines	28 (36)	11 (21)	39 (30)
EQ-5D VAS (scale range: 0-100), mean (SD)	70.0 (19.7)	73.3 (18.2)	71.4 (19.1)
FACT-Lym total (0-168), mean (SD)	116.1 (23.5)	121.5 (24.1)	118.4 (23.8)
Lymphoma subscale (0-60), mean (SD)	42.3 (10.5)	44.9 (10.1)	43.4 (10.3)
Trial outcome index (0-116), mean (SD)	77.4 (18.1)	83.1 (18.5)	79.8 (18.4)
FACT-G total (0-108), mean (SD)	73.9 (15.1)	77.0 (16.4)	75.2 (15.6)
Physical well-being (0-28), mean (SD)	21.1 (5.3)	23.1 (5.0)	21.9 (5.2)
Social/family well-being (0-28), mean (SD)	22.1 (4.9)	21.5 (6.8)	21.9 (5.7)
Emotional well-being (0-24), mean (SD)	16.9 (4.8)	16.9 (4.4)	16.9 (4.6)
Functional well-being (0-28), mean (SD)	14.1 (5.8)	15.6 (6.9)	14.8 (6.3)
Tumor response			
Overall response rate, n (%)	34 (44)	33 (62)	67 (52)

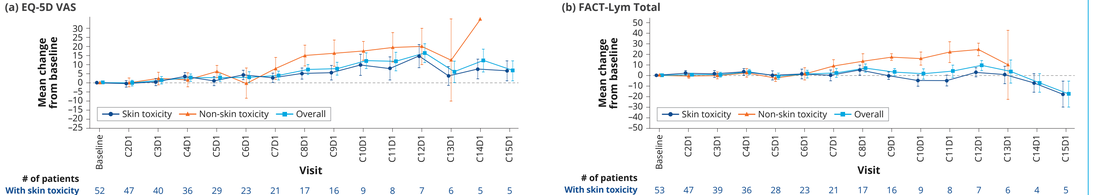
SD = standard deviation; VAS = visual analog scale.
Note: The sum of the percentages may not be 100 due to rounding.

Table 2. Least Squares Mean Differences (Without – With Skin Toxicity) in Change From Baseline Scores of EQ-5D VAS and FACT-Lym

	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1
EQ-5D VAS	−0.7	1.9	−0.4	6.2	−2.6	4.6	9.5	2.1
FACT-Lym total	−2.4	−1.7	1.0	−1.9	1.8	8.0	8.8	15.9[a]
Lymphoma subscale	−0.3	1.5	0.8	1.4	2.0	4.1	8.3	9.3
Trial outcome index	−0.5	−0.9	1.0	1.3	2.7	7.3	9.2	12.3
FACT-G total	−2.0	−3.1	0.1	−4.2	−1.5	1.4	−0.1	6.3
Physical well-being	−0.0	−0.4	−0.6	0.7	1.2	2.1	3.6	3.3
Social/family well-being	−1.6	−1.1	−0.7	−3.4	−1.8	−0.2	0.5	1.2
Emotional well-being	−0.1	0.5	1.0	1.0	0.5	1.2	−0.2	2.8
Functional well-being	−0.8	−1.1	0.5	−1.0	−1.3	−1.1	−2.6	−0.4

[a] $P < 0.05$.
Note: Age, sex, race, baseline score, and tumor response were adjusted in the analysis of covariance model. Visits after C9D1 are not displayed due to small sample sizes (n < 20). A positive difference is in favor of the group without skin toxicity.

Figure 2. Mean Change From Baseline in EQ-5D VAS and FACT-Lym Total by Visit and With/Without Skin Toxicity

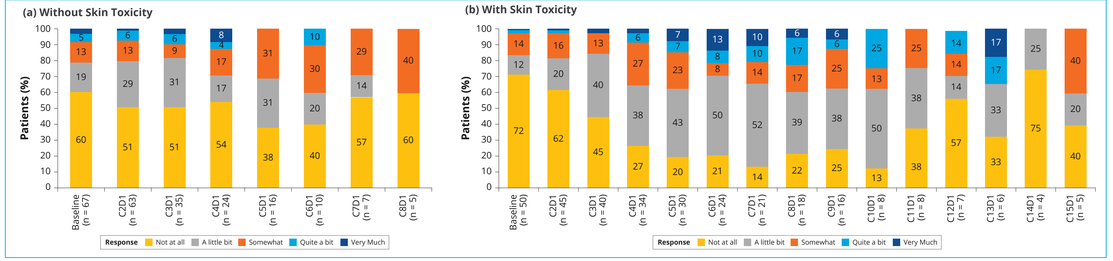


# of patients	Baseline	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1
With skin toxicity	52	47	40	36	29	23	21	17	16	9	8	7	6	5	5
Without skin toxicity	75	61	36	22	15	10	7	5	4	4	3	2	1		
Overall	127	108	76	58	44	33	28	22	20	13	12	10	8	6	5

# of patients	Baseline	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1
With skin toxicity	53	47	39	36	28	23	21	17	16	9	8	7	6	4	5
Without skin toxicity	72	59	35	23	15	10	7	5	4	4	4	3	3		
Overall	125	106	74	59	43	33	28	22	20	13	12	10	9	4	5

FACT-Lym = Functional Assessment of Cancer Treatment–Lymphoma; VAS = visual analog scale.
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 positive change indicates improvement.

Figure 3. Percentages of Responses to Item GP5 ("I am bothered by side effects of treatment") by Visit and With/Without Skin Toxicity



Notes: Later visits with fewer than 5 assessments are not displayed.

DISCUSSION

- In the analysis set of 130 patients, 53 patients experienced skin toxicity treatment-emergent adverse events (AEs) with a median 5 cycles of treatment (4 cycles among the 130 patients). The majority of patients (81%) experienced nonphotosensitivity cutaneous reactions. Although the analysis did not specifically align the timing of AEs with each patient-reported outcome assessment, the skin toxicity AEs often occurred after the first or second dose (the median start day was 32 days) and persisted for the duration of treatment (the median duration was 92 days, which was 4.4 cycles).
- When comparing patients with or without skin toxicity, there were no significant differences ($P > 0.05$) on adjusted mean change from baseline in overall health status (EQ-5D VAS), physical well-being, social/family well-being, emotional well-being, functional well-being, or lymphoma subscale after adjusting for age, sex, race, baseline score, and tumor response.
- Only at cycle 9 and only for FACT-Lym total, the adjusted mean change from baseline was significantly worse in the group with skin toxicity compared with the group without skin toxicity. However, there were only 4 patients remaining in the group without skin toxicity. Furthermore, as shown in Figure 2, the mean FACT-Lym total scores in the group with skin toxicity did not worsen compared with baseline.
- After 2 treatment cycles, a lower percentage of patients with skin toxicity reported they were "not at all" bothered by treatment side effects compared with those without skin toxicity. However, a majority of patients (≥ 60%) were either "not at all" or only "a little bit" bothered in both groups at each cycle.

CONCLUSIONS

- Patients with skin toxicity while receiving Lonca did not experience different HRQOL compared with patients without skin toxicity in most visits.
- Lonca was tolerated even among patients with skin toxicity.

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