Health-related quality of life, symptoms, and tolerability of loncastuximab tesirine in patients with relapsed or refractory diffuse large B-cell lymphoma

Alexander Spira
Xiaolei Zhou
Lei Chen
Ari Gnanasakthy
Luqiang Wang

See next page for additional authors
Authors
Alexander Spira, Xiaolei Zhou, Lei Chen, Ari Gnanasakthy, Luqiang Wang, David Ungar, Rafael Curiel, Laura Liao, John Radford, and Brad Kahl
Health-Related Quality of Life, Symptoms, and Tolerability of Loncastuximab Tesirine in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Alexander Spira,¹ Xiaolei Zhou,² Lei Chen,³ Ari Gnanasakthy,⁴ Luqiang Wang,⁵ David Ungar,³ Rafael Curiel,³,† Laura Liao,³ John Radford,⁴ Brad Kahl⁵

Abstract

This analysis evaluated the effects of loncastuximab tesirine on HRQoL, symptoms, and tolerability in patients with relapsed or refractory DLBCL, as observed in the single-arm, open-label phase II LOTIS-2 study. During treatment, improvement in EQ VAS overall health scores occurred over time and was associated with clinical response. FACT-Lym total scores remained stable during treatment.

Background: Loncastuximab tesirine has shown antitumor activity with an acceptable toxicity profile in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who were relapsed or refractory after ≥2 prior therapies, including activity in patients with high-risk disease characteristics. This analysis examined health-related quality of life (HRQoL), symptoms, and tolerability in patients receiving loncastuximab tesirine for relapsed or refractory DLBCL.

Patients and Methods: The single-arm, open-label phase II LOTIS-2 study (ADCT-402-201; NCT03589469) enrolled 145 patients aged ≥18 years. Patients received loncastuximab tesirine as a 30-minute intravenous infusion on day 1 of each 3-week treatment cycle. Patient-reported outcomes were measured using EQ-5D and FACT-Lym at baseline, day 1 of each cycle, and the end-of-treatment visit. Results: During the course of treatment, EQ VAS overall health score was improved over time. The adjusted improvement was 0.65 per cycle (95% CI, 0.26-1.04; P = .001), and the adjusted mean change from baseline score was 5.00 (95% CI, 1.75-8.25; P = .003) at cycle 9, day 1. FACT-Lym total scores remained stable during treatment. More patients reported improvement compared to baseline in pain, lumps/swelling, and losing weight for a majority of visits. More than 60% of patients reported being “not at all” or “a little bit” bothered by treatment side effects for all treatment visits. Findings in elderly patients were similar to the population as whole. Conclusion: The findings on HRQoL, symptoms, and tolerability further support the clinical use of loncastuximab tesirine for the treatment of relapsed or refractory DLBCL. Funding: This work was funded by ADC Therapeutics SA. Authors affiliated with ADC Therapeutics SA participated in designing the study; in collecting, analyzing, and interpreting the data; in writing the report; and in the decision to submit the article for publication.

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin’s lymphoma worldwide, representing approximately 30% to 40% of all cases in different geographic regions.¹ Chemoimmunotherapy, with or without radiotherapy, is the most common initial treatment for DLBCL.² The current standard of care for relapsed DLBCL is additional chemotherapy, which can

Keywords: Patient-reported, Clinical trial, Non-Hodgkin lymphoma, FACT-Lym, EQ-5D

Clinical Lymphoma, Myeloma and Leukemia, Vol. 22, No. 3, 158–168 © 2021 ADC Therapeutics. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Source(s) of Support: This study is sponsored by ADC Therapeutics SA; https://clinicaltrials.gov/ct2/show/NCT03589469.

¹Virginia Cancer Specialists, US Oncology Research, Johns Hopkins Medicine, Fairfax, VA
²RTI Health Solutions, Research Triangle Park, NC
³ADC Therapeutics America Inc., Murray Hill, NJ
⁴NHIR Manchester Clinical Research Facility, Christie NHS Foundation Trust and the University of Manchester, Manchester Academic Health Science Centre, Manchester UK
⁵Washington University School of Medicine in St. Louis, Saint Louis, MO

Submitted: Apr 29, 2021; Revised: Jul 13, 2021; Accepted: Sep 7, 2021; Epub: 22 September 2021

Address for correspondence: Lei Chen, PhD, ADC Therapeutics America Inc., Murray Hill, NJ

† Rafael Curiel was an employee of ADC Therapeutics when this research was conducted.

E-mail contact: Lei.Chen@adctherapeutics.com

2152-2650/$ - see front matter © 2021 ADC Therapeutics. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/) https://doi.org/10.1016/j.clml.2021.09.001
be followed by stem cell transplantation. The prognosis has been poor for patients with DLBCL who relapse or are refractory to treatment. The response rate for patients refractory to second-line or later-line therapy was 26%, with a median survival of 6.1 months. The poor prognosis for refractory or relapsed patients, especially those with chemotherapeutic refractory disease with a short interval between remission and relapse, highlights the unmet needs for patients with relapsed or refractory DLBCL.

In the ongoing, single-arm, phase II LOTIS-2 study, loncastuximab tesirine has shown antitumor activity, with an acceptable toxicity profile, in patients with relapsed or refractory DLBCL (following two or more systemic treatment regimens), including activity in patients with high-risk disease characteristics. Studies met the primary objective, showing an overall response rate of 48.3% (95% confidence interval [CI], 39.9%-56.7%); median duration of response was 10.3 months. Overall, 72.4% of patients had grade ≥3 treatment-emergent adverse events (most commonly, neutropenia, 25.5%; thrombocytopenia, 17.9%; increased gamma-glutamyltransferase, 16.6%; and anemia, 10.3%).

In addition to efficacy and toxicity, health-related quality of life (HRQoL) outcomes has been shown to be an important part of the evaluation of treatments, serve as a gauge of the value of the treatment in a uniquely patient-centric manner, and are increasingly recognized by stakeholders as a measure of value. The value of measuring HRQoL is important to supplement the efficacy evidence for patients with relapsed/refractory disease; however, to our knowledge, patient-reported tolerability of treatment side effects has not been reported in patients with relapsed or refractory DLBCL undergoing systemic therapy. As the number of therapy options for patients with relapsed or refractory DLBCL increases, choice of therapy is influenced by response and survival outcomes. However, patients’ HRQoL during treatment is also an important consideration in clinical decision-making, and HRQoL data for emerging therapies is often missing from the evidence base.

To further characterize the risk-benefit profile of loncastuximab tesirine, we conducted an analysis of patient-reported outcome (PRO) data from the LOTIS-2 study, with the objective of examining HRQoL, symptoms, and tolerability in patients receiving loncastuximab tesirine for relapsed or refractory DLBCL.

**Patients and Methods**

**Study Design and Patient Population**

LOTIS-2 (ADCT-402-201; NCT03589469) is a pivotal phase II, multicenter, single-arm, open-label study of adult patients with relapsed or refractory DLBCL. Patients must have a pathologic diagnosis of DLBCL (as defined by the 2016 World Health Organization classification; including DLBCL not otherwise specified, high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements, and primary mediastinal B-cell lymphoma) that was relapsed or refractory following two or more systemic treatment regimens. Enrolled patients received loncastuximab tesirine as a 30-minute intravenous infusion on day 1 of each 3-week treatment cycle at a dose of 150 μg/kg for 2 cycles and then 75 μg/kg for subsequent cycles. Patients also received dexamethasone premedication 1 day prior to, the day of, and 1 day after the infusion of loncastuximab tesirine. Patients could continue treatment until disease progression, unacceptable toxicity, or other discontinuation criteria were met. The study protocol was approved according to local regulations from the appropriate institutional review board/independent ethics committee. Informed consent was obtained for each patient and documented with a signed informed consent form prior to any study procedures.

**Patient-Reported Outcome Assessments**

Patient-reported outcomes were measured by EQ-5D 5 Levels (EQ-5D-5L) and the Functional Assessment of Cancer Treatment–Lymphoma (FACT-Lym) instruments at baseline (cycle 1, day 1 predose), day 1 of each subsequent treatment cycle, and at the end-of-treatment visit. Both instruments are widely used and have been validated. The EQ-5D-5L is an international, standardized, generic instrument for describing and evaluating health status and utility. Overall health (current health state) was measured by the EQ visual analog scale (EQ 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 is commonly used for patients with lymphoma. It consists of a generic core questionnaire, the Functional Assessment of Cancer Therapy–General (FACT-G, 27 items) and a Lymphoma Subscale (LymS, 15 items) specifically for evaluating response to treatment in patients with non-Hodgkin’s lymphoma. The recall period is the past 7 days. The FACT-G total score (range, 0–108) is the sum of 4 well-being (WB) scores: 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). The LymS score (range, 0–60) is a summary score of 9 items of symptoms or bothersome by symptoms (pain, lumps or swelling, fever, night sweat, weight loss, itching, trouble sleeping, fatigue, and loss of appetite) and additional items of patients’ concerns. Items were measured on a 5-point Likert scale. The item response scores for negatively phrased questions were reversed before summing. The summary scores FACT-Lym trial outcome index (TOI = physical WB + functional WB + LymS) and FACT-Lym total (= FACT-G total + LymS) were also derived. For each of the composite scores, 0 indicates worse HRQoL, and higher scores indicate better HRQoL. The maximum score varies depending on the total number of items in the components of each score. Items missing data were handled following the instrument developer’s user manual.

Patient-reported tolerability was assessed using the FACT-Lym item GSP (“I am bothered by side effects of treatment”). This single item provides a measure of overall side effect impact on patients. It was shown to be significantly associated with clinician-reported adverse events and with patients’ ability to enjoy their lives. It was also discussed in a recent FDA-ASCO public workshop (2020 Clinical Outcome Assessments in Cancer Clinical Trials Fifth Annual Workshop).

**Analysis Methods**

Change from baseline scores in EQ VAS and FACT-Lym were among the secondary endpoints of the LOTIS-2 study to evaluate the impact of loncastuximab tesirine treatment on HRQoL with descriptive analysis. The change from baseline scores were summarized by study visits (cycles) along with the standard errors.
Percentages of patients with improvement or deterioration based on minimally important difference (MID) were also summarized for EQ VAS. Change of 7 points from baseline on the EQ VAS was considered MID. Post hoc mixed models were conducted for change from baseline scores, with visit and baseline score as the fixed effect and intercept as the random effect. Change from baseline scores at the first postbaseline visit (cycle 2, day 1) and the last visit with a decent sample size (cycle 9, day 1, n = 20) were estimated along with the 95% CIs. The slope for visit (change in scores per cycle) was also estimated. Additionally, change from baseline scores were summarized by clinical response (responders were patients with a best overall response of complete or partial response), and a subgroup analysis was conducted for elderly patients (≥65 years).

We further conducted exploratory analyses for nine items of either symptoms or bother by the associated symptoms related to non-Hodgkin’s lymphoma or treatment for the disease and the tolerability item (GP5). Because the symptoms were measured on a 5-point Likert scale, percentages of patients with improved (by at least 1 point), stable, or worsened (by at least 1 point) symptoms compared with baseline were calculated. The Wilcoxon signed rank test, a nonparametric test for paired ordinal variables, was conducted to test the difference between the symptom scores before and after receiving the treatment. Percentages of responses to GP5 (tolerability) were summarized by visits.

The analysis was conducted by using data collected from study initiation (August 1, 2018) through April 6, 2020. We tabulated the compliance rate for PRO data at each visit. Data were analyzed as observed. To investigate the potential impact of missing data, we examined the reason for missing data. P values for all analyses were provided as exploratory analysis without adjustment for multiple comparison.

### Results

The study enrolled 145 patients with refractory or relapsed DLBCL. Histologies were DLBCL, not otherwise specified (87.6%); high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (7.6%); and primary mediastinal large B-cell lymphoma (4.8%). One-fifth (20.0%) of the patients had transformed disease, and 10.3% had double-hit or triple-hit disease. The majority had advanced disease (64.1% stage IV and 13.1% stage III). The study population was 59% men and 90% white. The median age was 66 years (range, 23-94 years); 55% were elderly (aged ≥65 years), and 14% were aged at least 75 years. Patients were heavily pretreated, with a median of three prior systemic therapies (range, 2-7 therapies); 24 patients (16.6%) had received prior stem cell transplant (21 autologous, 2 allogeneic, and 1 both), and 13 patients (9%) had received CAR-T therapy. In the study, patients had received a median of 3 (range, 1-15) cycles of loncastuximab tesirine as of the data cutoff, with 8 patients still on treatment.

A baseline PRO score and at least one postbaseline score were available for 130 patients in the PRO analysis set (Figure 1). As shown in Table 1, completion rates among patients treated at each visit were ≥92% for EQ-5D-5L and ≥88% for FACT-Lym up to cycle 9, day 1 (24 weeks after the first dose on cycle 1, day 1). After cycle 9, fewer than 20 patients had PRO scores available for analysis.

### EQ VAS and FACT-Lym Scores

The mean (standard deviation) EQ VAS score was 71.4 (19.1) at baseline. The mean change from baseline in EQ VAS score showed a trend of improvement in the overall population in overall health over time (Figure 2A). The mean change in EQ VAS score was above 0 starting from cycle 3, day 1, and reached the MID of 7 points at cycle 8. Although the sample size reduced considerably compared with baseline, the remaining patients after cycle 9 had even higher mean change from baseline score in EQ VAS. Results from a mixed model that adjusted for baseline score are shown in Table 2. The adjusted improvement on EQ VAS overall health was 0.65 per cycle (95% CI, 0.26-1.04, P = .001). At cycle 9, day 1, the adjusted mean change from baseline score was 5.00, close to the MID (95% CI, 1.75-8.25, P = .003).

Similarly, at each visit during treatment, a higher percentage of patients experienced meaningful improvement than they did deterioration (Figure 2B). For example, at cycle 9, day 1, only 15% of patients experienced meaningful deterioration, 40% remained stable, and 45% experienced meaningful improvement (30 percentage points higher than the percentage deterioration).

Descriptive summaries of the FACT-Lym WB and composite scores are provided in Table S1 and Figure S1 (Supplemental Appendix). During treatment, all FACT-Lym WB and composite scores remained stable in overall patient population except for worsened social/family WB at some visits. Results from mixed models adjusting for baseline scores are presented in Table 2. Compared with baseline, there was no meaningful or statistically significant change in physical WB, TOL, and FACT-Lym total scores. The emotional WB and LymS scores were statistically improved, as shown in the small P values for cycle 2, day 1 and/or cycle 9, day 1, but the magnitude of the improvement was not meaningful. Social/family WB and functional WB declined slightly over time. The FACT-G total score (the sum of physical, social/family, emotional, and functional WB) generally remained stable.

### Table 1: Completion Rate for EQ-5D and FACT-Lym Scores by Visit

<table>
<thead>
<tr>
<th>Visit</th>
<th>EQ-5D</th>
<th>FACT-Lym</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>141/145 (97.2)</td>
<td>136/145 (93.8)</td>
</tr>
<tr>
<td>Cycle 2, Day 1</td>
<td>115/120 (95.8)</td>
<td>112/120 (93.3)</td>
</tr>
<tr>
<td>Cycle 3, Day 1</td>
<td>81/87 (93.1)</td>
<td>78/87 (89.7)</td>
</tr>
<tr>
<td>Cycle 4, Day 1</td>
<td>63/68 (92.6)</td>
<td>61/68 (89.7)</td>
</tr>
<tr>
<td>Cycle 5, Day 1</td>
<td>46/49 (93.9)</td>
<td>43/49 (87.8)</td>
</tr>
<tr>
<td>Cycle 6, Day 1</td>
<td>34/36 (94.4)</td>
<td>34/36 (94.4)</td>
</tr>
<tr>
<td>Cycle 7, Day 1</td>
<td>29/29 (100.0)</td>
<td>28/29 (96.6)</td>
</tr>
<tr>
<td>Cycle 8, Day 1</td>
<td>23/25 (92.0)</td>
<td>22/25 (88.0)</td>
</tr>
<tr>
<td>Cycle 9, Day 1</td>
<td>20/20 (100.0)</td>
<td>20/20 (100.0)</td>
</tr>
<tr>
<td>Cycle 10, Day 1</td>
<td>12/14 (85.7)</td>
<td>12/14 (85.7)</td>
</tr>
<tr>
<td>Cycle 11, Day 1</td>
<td>9/11 (81.8)</td>
<td>9/11 (81.8)</td>
</tr>
<tr>
<td>Cycle 12, Day 1</td>
<td>8/11 (72.7)</td>
<td>8/11 (72.7)</td>
</tr>
<tr>
<td>Cycle 13, Day 1</td>
<td>6/7 (85.7)</td>
<td>6/7 (85.7)</td>
</tr>
</tbody>
</table>

The denominator is the number of patients treated at a visit. Fewer than 5 patients were treated after cycle 13.
Figure 1  CONSORT flow diagram. * Including one patient who checked other reason but specified as stem cell transplant.

PRO = patient-reported outcome.
While there was no obvious difference in baseline scores between responders and nonresponders (Table S1, Supplemental Appendix), the improvement in EQ VAS was associated with clinical response (Figure 2). The mean change from baseline VAS score increased over time among responders. Among nonresponders, it was maintained without deterioration. Most FACT-Lym WB and composite scores remained stable among responders and declined among nonresponders (Figure S1, Supplemental Appendix).

**Symptoms**

Of the symptoms assessed in the LymS of FACT-Lym, pain in certain parts of the body, being bothered by lumps/swelling, trouble sleeping at night, and fatigue (“get tired easily”) were the most frequently reported at baseline (33%-59% reported “somewhat” to “very much,” Table S2, Supplemental Appendix). Most patients (≥80%) reported “not at all” or “a little bit” at baseline for being bothered by fever, night sweats, losing weight, itching, and
Figure 2  Continued

(b) Percentage of clinically meaningful improvement, no change, and deterioration

Table 2  Results From Mixed Models for EQ VAS and FACT-Lym Change Scores

<table>
<thead>
<tr>
<th></th>
<th>MID Prespecified Threshold (Range of Threshold)</th>
<th>Change From Baseline to C2D1</th>
<th>Change From Baseline to C9D1</th>
<th>Change per Cycle (Slope)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Est. (95% CI)</td>
<td>P Value</td>
<td>Est. (95% CI)</td>
</tr>
<tr>
<td>EQ VAS</td>
<td>7</td>
<td>0.42 (-2.20 to 3.04)</td>
<td>.749</td>
<td>5.00 (1.75-8.25)</td>
</tr>
<tr>
<td>FACT-Lym physical well-being</td>
<td>2.5 (2-3)</td>
<td>-0.24 (-0.95 to 0.46)</td>
<td>.494</td>
<td>-0.03 (-0.93 to 0.86)</td>
</tr>
<tr>
<td>FACT-Lym social/family well-being</td>
<td>Not available</td>
<td>-0.43 (-1.30 to 0.44)</td>
<td>.330</td>
<td>-1.46 (-2.53 to -0.38)</td>
</tr>
<tr>
<td>FACT-Lym emotional well-being</td>
<td>(21)</td>
<td>0.69 (0.12-1.25)</td>
<td>.018</td>
<td>0.80 (0.08-1.52)</td>
</tr>
<tr>
<td>FACT-Lym functional well-being</td>
<td>2.5 (2-3)</td>
<td>0.32 (-0.64 to 1.29)</td>
<td>.506</td>
<td>-1.18 (-2.35 to -0.01)</td>
</tr>
<tr>
<td>FACT-Lym LymS</td>
<td>3 (2.9-5.4)</td>
<td>1.36 (0.16-2.57)</td>
<td>.027</td>
<td>1.33 (-0.15 to 2.81)</td>
</tr>
<tr>
<td>FACT-G Total Score</td>
<td>3 (3-7)</td>
<td>0.12 (-2.09 to 2.32)</td>
<td>.917</td>
<td>-1.79 (-4.50 to 0.92)</td>
</tr>
<tr>
<td>FACT-Lym TOI</td>
<td>6 (5.5-11)</td>
<td>0.94 (-1.46 to 3.34)</td>
<td>.439</td>
<td>-0.04 (2.95 to 2.87)</td>
</tr>
<tr>
<td>FACT-Lym Total Score</td>
<td>7 (6.5-11.2)</td>
<td>0.93 (-2.10 to 3.95)</td>
<td>.546</td>
<td>-0.91 (-4.57 to 2.76)</td>
</tr>
</tbody>
</table>

TOI = Trial outcome index = physical well-being + functional well-being + LymS

* This MID should be considered tentative, as it may be revised based on future research.  For higher scores indicate better quality of life.
loss of appetite. During the course of treatment (Figure 3), more patients reported improvement compared with baseline for pain, lumps/swelling, and losing weight for a majority of the visits (percentage of patients with improvement – percentage of patients with symptom worsening >10 percentage points for a majority of the visits, and $P < .05$ or .10 for Wilcoxon signed rank test at several visits). Fever and night sweats did not change for most patients. Itching was the only symptom for which more patients experienced worsening with $P$ value >.10 except one visit ($P = .06$ at cycle 7, day 1). For other symptoms (fatigue, trouble sleeping, and loss of appetite), there was no clear trend for improvement or worsening.
**GP5-Based Patient-Reported Tolerability to Treatment**

When patients were asked how much they were bothered by the side effects of treatment at baseline (Figure 4), 81% reported “not at all” or “a little bit,” and 5% reported “quite a bit” or “very much.” This likely reflects residual side effects from previous treatments. Throughout all visits during treatment, most patients (>60%) reported being “not at all” or “a little bit” bothered by side effects of treatment.

**Elderly Patients**

More than half of the study population was elderly patients (aged ≥65 years). Results for HRQoL, symptoms, and tolerability were very similar to those for the overall population. Specifically, during treatment with loncastuximab tesirine, higher percentages of patients reported improvement for pain, lumps/swelling, and losing weight for the majority of visits. Itching was the only symptom for which more patients experienced worsening rather than improvement. The EQ VAS overall health score and most FACT-Lym scores were maintained or improved among elderly patients. The majority of elderly patients reported treatment tolerability (Figure 5).

**Discussion**

In this analysis, patients with relapsed or refractory DLBCL enrolled in the LOTIS-2 study completed the FACT-Lym and EQ-5D-5L at the beginning of each treatment cycle of loncastuximab tesirine. Over the course of the treatment, overall HRQoL was maintained or improved, especially among patients with complete or partial response. Mean changes from baseline scores in the EQ VAS were consistently greater than 0 starting from cycle 3, day 1 (with 40% improved by at least the MID), suggesting positive improvement in overall health as early as after 2 cycles of loncastuximab tesirine treatment. Mean change scores gradually increased to MID and above after 7 cycles of treatment, with all patients remaining at cycle 8 or later being responders except for one nonresponder. Patients remaining at cycle 9, day 1 (Table S3, Supplemental Appendix) included elderly patients (40% aged 65 to <75 years and 20% aged 75 years or older) and patients who were heavily pretreated (30% with >3 prior lines of systemic therapies). Comparing with the baseline, FACT-Lym total score was maintained in the overall patient population, despite some WBs having improved and some having declined. A possible explanation for the different trends observed between PRO measures, with the EQ VAS showing improved HRQoL and the FACT-Lym showing maintained HRQoL, is that these measures assess different aspects of the patient experience. EQ VAS is a single item assessing overall health state, while FACT-Lym consists of 27 items for physical, social/family, and emotional and functional well-being and 15 items for lymphoma-specific items.

Consistently higher proportions of patients reported improvement compared with baseline for pain, lumps/swelling, and losing weight for a majority of visits. Itching was the only symptom for which more patients experienced worsening. This is consistent with
Health-Related Quality of Life, Symptoms, and Tolerability

Figure 5 Overall health and tolerability among elderly patients (aged ≥65 y). (A) Change from baseline scores in EQ VAS by visit. (B) Percentages of responses to GP5 (“I am bothered by side effects of treatment”) by visits. VAS = visual analog scale.

(a) Change from baseline scores in EQ VAS by visit

(b) Percentages of responses to GP5 (“I am bothered by side effects of treatment”) by visits

VAS = visual analog scale.
loncastuximab tesirine’s known toxicity profile: 43% experienced skin- or nail-related toxicities, which were generally mild to moderate in severity (4% grade ≥3). Furthermore, most patients reported being able to tolerate treatment-related toxicity. Results were very similar among elderly patients as well.

The FACT-Lym item GP5 (“I am bothered by side effects of treatment”) is one of the items included in the physical WB subscale. It is rated on a 5-point Likert scale from “not at all” to “very much.” This single item was shown to be significantly associated with clinician-reported adverse events and with patients’ ability to enjoy their lives. Therefore, it is proposed as an overall summary measure of the burden of treatment toxicities. More than 60% of patients receiving loncastuximab tesirine reported “not at all” or “a little bit” for all visits throughout treatment. In addition to the adverse events assessed by clinicians, this provides evidence of tolerability to loncastuximab tesirine, which was directly reported by patients. These favorable findings based on PRO endpoints further complement the efficacy and safety evidence for loncastuximab tesirine to inform decision making as the therapeutic landscape evolves.

Existing evidence on the impact of treatment on the HRQoL of patients with relapsed or refractory DLBCL is limited and has yielded inconsistent findings. Patients newly diagnosed with DLBCL and those with relapsed or refractory disease show considerable deficiency in HRQoL at the time of diagnosis and after all treatments. HRQoL in patients diagnosed with relapsed or refractory DLBCL is lowest after their first treatment cycle and is impacted by treatment-related adverse events. Patients with relapsing or refractory DLBCL who responded to treatment with tisagenlecleucel therapy (ie, a responder population) showed clinically meaningful improvement in domains of HRQoL and sustained their level of improvement during an 18-month long-term follow-up. In the maintenance setting, HRQoL was not negatively affected by treatment with lenalidomide in patients with relapsing or refractory DLBCL. However, a recent review of 26 studies reporting HRQoL in patients with relapsed or refractory DLBCL from 2007 to 2019 showed that patients report decreases in HRQoL while receiving their therapies.

Due to the study’s single-arm and open-label design, caution should be used when comparing the findings of this study with other studies of other treatments. Patients’ perceptions of symptoms and treatment tolerability as reflected by the PRO measures collected in this study may have been influenced by their knowledge of the treatment they were taking. As is commonly seen in oncology clinical studies, the number of completed PRO assessments reduced over time; this may bias the overall population (eg, data on the later cycles were enriched with responders). Most of the missing data were due to treatment termination. At the time of data cut, 137 patients (94.5%) had terminated the treatment because of progressive disease (55.9%), toxicity (20.7%), death (6.2%), or other reasons (11.7%). The median number of treatment cycles administered was 3.0 (range, 1-15). When examining the impact of missing data on EQ VAS, no significant difference was found between patients with >3 or ≤3 cycles of therapy in the mean change from baseline EQ VAS scores at cycle 2 day 1 and cycle 3 day 1. The limitations of the EQ VAS as a measure of health status also must be considered; in particular, the measure has a 1-day recall but was administered every 3 weeks. Among patients who were treated at a visit, the compliance rate of PRO assessments was nearly 90% or higher, although we cannot rule out the possibility that patients who were sicker were less likely to complete the PRO assessments. Therefore, our analyses were limited to the time when patients were on treatment and should not be generalized post loncastuximab tesirine treatment. Despite these limitations, a strength of our analysis is the frequent evaluation of symptoms, HRQoL, and tolerability among the LOTIS-2 PRO-evaluable population in addition to an analysis of HRQoL among patients responding to treatment. Taken together, our results suggest that overall health showed a trend of improvement while patients were on treatment and improved among those with a complete or partial tumor response.

Conclusions

Results of this analysis suggest that patients with relapsed or refractory DLBCL who were on treatment with loncastuximab tesirine, including elderly patients, had stable or improved overall HRQoL, especially among responders. More patients reported improvement in symptoms of pain, lumps/swelling, and weight loss compared with baseline for a majority of visits. The treatment was well tolerated as reported by a majority of patients. These findings further support the clinical use of loncastuximab tesirine for the treatment of relapsed or refractory DLBCL.

Clinical Practice Points

What is Already Known About this Subject?

• DLBCL is the most common type of non-Hodgkin’s lymphoma worldwide. The prognosis has been poor for patients with DLBCL who relapse or are refractory to initial treatment. In addition to the efficacy and toxicity of a treatment, HRQoL outcomes have served as a gauge for the value of the treatment in a uniquely patient-centric manner, and they are increasingly recognized by various stakeholders as a measure of value.

• In the ongoing, single-arm, phase II LOTIS-2 study, loncastuximab tesirine monotherapy has shown substantial antitumor activity with a manageable toxicity profile in patients with relapsed or refractory DLBCL.

What are the New Findings?

• HRQoL was maintained or improved in patients who received treatment. The EQ VAS overall health score was improved over time, with an adjusted improvement of 0.65 per cycle (95% CI, 0.26-1.04, P = .001) and an adjusted mean change from baseline of 5.00 (95% CI, 1.75-8.25, P = .003) at cycle 9, day 1. This improvement was associated with clinical response. FACT-Lym total score remained stable.

How Might the Results Impact on Clinical Practice in the Foreseeable Future?

• The importance of HRQoL in oncology trials is often underappreciated. Clinical studies have shown that loncastuximab tesirine has antitumor activity and a manageable toxicity profile. This analysis demonstrates that patients with relapsed or refractory DLBCL who received treatment had maintained or improved overall HRQoL. These findings further support the clinical use
Disclosure

The LOTIS-2 (ADCT-402-201) trial was funded by ADC Therapeutics. The analysis reported here was performed under a research contract between ADC Therapeutics and RTI Health Solutions and was funded by ADC Therapeutics. XZ and AG are employees of RTI Health Solutions. LC, LW, DU, and LL are employees of ADC Therapeutics. RC is a former employee of ADC Therapeutics. BK has received consulting fees from ADC Therapeutics. AS has received institutional research support from ADC Therapeutics. JR has received honoraria from ADC Therapeutics for taking part in advisory boards and is an ADC Therapeutics stockholder.

Acknowledgments

Medical writing services were provided by Kate Lothman of RTI Health Solutions. These services were funded by ADC Therapeutics.

Supplementary materials


References