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Patient-reported long-term quality of life after tisagenlecleucel in relapsed/refractory diffuse large B-cell lymphoma

Richard T. Maziarz,[1] Edmund K. Waller,[2] Ulrich Jaeger,[3] Isabelle Fleury,[4] Joseph McGuirk,[5] Harald Holte,[6,7] Samantha Jaglowski,[8,9] Stephen J. Schuster,[10] Michael R. Bishop,[11] Jason R. Westin,[12] Stephan Mielke,[13-15] Takanori Teshima,[16] Veronika Bachanova,[17] Stephen R. Foley,[18] Peter Borchmann,[19] Gilles A. Salles,[20] Jie Zhang,[21] Ranjan Tiwari,[22] Lida B. Pacaud,[21] Qiufei Ma,[21] and Constantine S. Tam[23]

[1]Center for Hematologic Malignancies, Oregon Health and Science University (OHSU) Knight Cancer Institute, Portland, OR; [2]Bone Marrow and Stem Cell Transplant Center, Winship Cancer Institute of Emory University, Atlanta, GA; [3]Division of Hematology and Hemostaseology, Department of Medicine I, Medical University of Vienna, Vienna, Austria; [4]Maisonneuve-Rosemont Hospital, University of Montreal, Montreal, QC, Canada; [5]Department of Blood and Bone Marrow Transplant, The University of Kansas Cancer Center, Kansas City, KS; [6]Department of Oncology, Oslo University Hospital, Oslo, Norway; [7]K.G. Jebsen Centre for B cell Malignancies, Oslo, Norway; [8]The James Cancer Hospital and [9]Solove Research Institute, The Ohio State University Comprehensive Cancer Center, Columbus, OH; [10]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [11]Section of Hematology/Oncology, Department of Medicine and Comprehensive Cancer Center, University of Chicago, Chicago, IL; [12]Department of Lymphoma and Myeloma, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; [13]Department of Cellular Therapy and Allogeneic Stem Cell Transplantation (CAST), Karolinska Institutet, Stockholm, Sweden; [14]Department of Laboratory Medicine, Karolinska University Hospital, Stockholm, Sweden; [15]Center for Allogeneic Stem Cell Transplantation, Department of Internal Medicine II, Würzburg University Medical Center, Würzburg, Germany; [16]Department of Hematology, Hokkaido University Hospital, Sapporo, Japan; [17]Division of Hematology, Oncology, and Transplantation, Department of Medicine, University of Minnesota, Minneapolis, MN; [18]Juravinski Hospital and Cancer Centre, McMaster University, Hamilton, ON, Canada; [19]Department of Haematology and Oncology, University Hospital of Cologne, Cologne, Germany; [20]Department of Hematology, Centre Hospitalier Lyon-Sud Hospital, Hospices Civils de Lyon, University of Lyon, Lyon, France; [21]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [22]Novartis Healthcare Pvt. Ltd, Hyderabad, India; and [23]Peter MacCallum Cancer Centre, St Vincent's Hospital and University of Melbourne, Melbourne, VIC, Australia

Key Points

- Tisagenlecleucel demonstrated clinically meaningful and sustained improvements in HRQoL among responding patients with r/r DLBCL.

The JULIET phase 2 trial evaluated a single infusion of tisagenlecleucel in adult patients with relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL). The objective of the current analysis was to evaluate patient-reported health-related quality of life (HRQoL) with a median follow-up of 19.3 months among patients infused with a single dose of tisagenlecleucel. Patients enrolled were ≥18 years of age with r/r DLBCL after ≥2 lines of therapy and had either undergone a failed autologous stem cell transplant or were ineligible for the procedure. Two validated HRQoL instruments, Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym) and Short Form-36 (SF-36) Health Survey, were used to measure HRQoL at baseline and months 3, 6, 12, and 18. At data cutoff (21 May 2018), 115 patients had received tisagenlecleucel infusion. Among the 99 patients evaluated, overall response rate was 54%, and 40% of patients achieved complete response (CR). Initially, 108 patients completed the HRQoL assessments at baseline, including 57 patients who eventually achieved CR or partial response (PR). Further, 30 and 21 patients in clinical response who completed assessments at baseline also completed assessments at months 12 and 18, respectively. Patients who achieved CR or PR sustained HRQoL improvement in all FACT scores at all time points. SF-36 instruments showed improvement above the minimal clinically important differences on 5 of 8 subscales. Long-term follow-up in the phase 2 JULIET study demonstrated that patients with r/r DLBCL who respond to tisagenlecleucel therapy had sustained, clinically meaningful improvements in HRQoL. This trial was registered at www.clinicaltrials.gov as #NCT02445248.

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Novartis is committed to sharing, with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided are anonymized to respect the privacy of patients who have participated in the trial, in line with applicable laws and regulations. The availability of these trial data is according to the criteria and process described on www.clinicalstudydatarequest.com.

The full-text version of this article contains a data supplement.

Introduction

The prognosis has been poor for patients with diffuse large B-cell lymphoma (DLBCL) who relapsed or were refractory to treatment. Salvage therapy for refractory non-Hodgkin lymphoma has been associated with an overall response rate (ORR) and complete response (CR) of 26% and 7%, respectively; median overall survival (OS) was 6 months, with a 2-year OS of 20%.[1] Tisagenlecleucel (KYMRIAH) is an immunocellular therapy that uses autologous peripheral blood T cells, genetically modified ex vivo (chimeric antigen receptor [CAR] T cells), to target CD19 on the surface of B cells. Tisagenlecleucel was approved for pediatric and young adult relapsed/refractory (r/r) acute lymphoblastic leukemia (ALL) and for adult r/r DLBCL in the United States, Europe, Japan, Canada, and Australia.[2-5]

In the JULIET trial, at a median follow-up of 19 months, the ORR in adult patients with r/r DLBCL was 54% (95% confidence interval [CI], 43%-64%) with 40% of patients achieving a CR among the 99 patients evaluable for efficacy. The ORR was similar across prognostic subgroups including patients with prior autologous stem cell transplant (ASCT) and those with double/triple-hit lymphoma. Fifteen patients had a partial response (PR) converted to a CR (54%, 15/28). The median duration of response has not been reached at this cutoff (95% CI, 10.0 months to not evaluable [NE]). Overall, the duration of response was similar between age subgroups (≥65 years vs <65 years) and r/r status. The median OS was 11.1 months (95% CI, 6.6 months to NE) in the overall patient population and not reached for patients with a CR (95% CI, 21.1 months-NE). Overall, tisagenlecleucel therapy was associated with manageable adverse events, and the most common grade 3 or 4 adverse events of special interest included cytokine release syndrome (23%), neurologic events (11%), cytopenias lasting >28 days (34%), infections (19%), and febrile neutropenia (15%).

To complement the primary efficacy and safety analyses and in view of the innovative nature of CAR T-cell therapy in r/r DLBCL, patient-reported outcomes (PROs) were also assessed. Quality-of-life (QOL) outcomes have been shown to be important determinants for defining which treatments should be used in clinical practice because they have provided a measure of clinical effectiveness, served as a gauge of the value of the treatment in a uniquely patient-centric manner, and are increasingly recognized as value measures by payers.[6-8] Yet, health-related QoL (HRQoL) data in patients with r/r DLBCL are surprisingly limited.

Preliminary analyses of the JULIET trial showed clinically meaningful improvements in HRQoL at months 3 and 6, compared with baseline among patients who achieved a CR or PR.[9] In this report, the long-term HRQoL outcomes of the JULIET trial establish a benchmark of PROs for patients with r/r DLBCL who have received ≥2 lines of therapy and for CAR T-cell therapy.

Methods

Study design and patients

JULIET is a global, single, open-label, phase 2 study of tisagenlecleucel in adult patients with r/r DLBCL; details of the study design have been described.[10] In brief, eligible patients were ≥18 years of age and had ≥2 lines of prior therapy including rituximab and anthracycline. Patients had either relapsed after or were ineligible for ASCT. Participants also included those with DLBCL that transformed from follicular lymphoma or with high-grade B-cell lymphoma with *MYC* rearrangements, plus rearrangement of *BCL2*, or *BCL6*, or a combination of these genes (double- or triple-hit lymphoma). Patients were excluded if they had prior CD19-directed therapy, primary mediastinal DLBCL, prior allogenic stem cell transplantation, or active central nervous system involvement stemming from DLBCL.

Data collection and patient-reported QoL assessments

Patients self-administered and completed the Function Assessment of Cancer Therapy-Lymphoma (FACT-Lym) and the Short Form 36 Health Survey Version 2 (SF-36) questionnaires (see supplemental Data).[11,12] Data were collected before clinical assessments and before the patients received any study medications or therapies. Patient-reported HRQoL was assessed at baseline (screening phase) and months 3, 6, 12, and 18, using validated instruments for FACT-Lym and SF-36.

FACT-Lym is a questionnaire used to assess the QoL in patients with lymphoma and included the FACT-General (FACT-G) and the lymphoma subscale (Lym S).[11] The FACT-G is composed of 27 general questions in 4 primary HRQoL domains: physical, social/family, emotional, and functional well-being. The FACT-G questionnaire has been applied in previous studies to assess the HRQoL of patients with lymphoma.[13-18] Lym S is a 15-question survey focusing on patient response to lymphoma-associated treatment and symptoms, along with other concerns (score range, 0-60). Disease and treatment-related symptoms assessed by the questionnaire include pain, fever, swelling, night sweats, insomnia, itching, weight loss, fatigue, and loss of appetite. FACT summary scores were determined by adding various domains as follows: FACT-G total score included physical, social/family, emotional, and functional well-being (score range, 0-108), the FACT-Lym Trial Outcome Index (TOI) included physical and functional well-being and Lym S (score range, 0-116), and the FACT-Lym total score included the FACT-G total plus Lym S (score range, 0-168).

Patient-reported HRQoL was also assessed using the SF-36 questionnaire, which has become the standard for HRQoL across general and disease populations, including patients with non-Hodgkin lymphoma.[12,19-21] The assessment of SF-36 consists of 8 subscales that generate a profile of HRQoL that is used in healthy individuals and in patients with acute and chronic conditions.[12] The subscales are composed of physical functioning, role limitations because of emotional and physical health problems, physical pain, general health perception, vitality, social functioning, and mental health. Each subscale was scored individually, and 2 overall summary scores for the physical component and the mental component were generated (score range, 0-100).

For both instruments, FACT-Lym and SF-36, a score of 0 indicated the worst HRQoL, whereas higher scores equated to improved HRQoL. Although the instruments had a few overlapping questions, both questionnaires were used to maximize the data captured from patients.

Study-specific HRQoL data and patient-reported outcomes were no longer collected when patients developed progressive disease

during the study and transitioned to alternative treatment plans or supportive care only.

Statistical methods

As a prespecified exploratory end point in the JULIET study, the summary scores (FACT-Lym total score, SF-36 physical health total score, and SF-36 mental health total score) were generated by summing the item responses on the questions for each domain, in accordance with the respective scoring manual provided by the HRQoL instrument developers. A proprietary algorithm based on a factor analytic technique that forces the scores to be orthogonal was used to calculate the SF-36 scores (OPTUM, Eden Prairie, MN).[22,23]

Descriptive statistics (eg, mean, median, and frequency) and change from baseline of the summary scores for each postbaseline time point or window of assessment were provided based on all available data at the time of final analysis. For instance, mean changes from baseline in FACT-Lym and SF-36 were calculated at the 3-, 6-, 12-, and 18-month postbaseline visits.

Minimally clinically important differences (MCIDs) were identified using both anchor- and distribution-based methods[15,24] and were estimated to range from 2.9 to 5.4 for the FACT-Lym S, 5.5 to 11 for the FACT-Lym TOI, 6.5 to 11.2 for the FACT-Lym TS, and 3 to 7 for the FACT-G TS.[11,15,25] For the SF-36, MCIDs were estimated to be 3 for the physical component score, mental component score, and vitality subscale; 4 for the role-emotional, role-physical, and social-functioning subscales; and 2 for the general health subscale.[26] Patient-reported outcome assessment completion was conducted as a post hoc analysis, given that most of the completed assessments were from patients who achieved CR or PR.

The study protocol was approved by the institutional review board at each participating institution. Data were analyzed and interpreted by Novartis and the authors.

Results

Patients

At the time of data cutoff (21 May 2018), 115 of 167 patients with r/r DLBCL were infused with tisagenlecleucel (99 patients in the main cohort manufactured in the United States and 16 patients in cohort A manufactured in Germany).[27,28] The median age of infused patients was 56 years (range, 22-76), and 23% were ≥65 years of age. Of the 115 patients, 96% had received ≥2 systemic therapies, and 49% relapsed after ASCT (Table 1).[10,27,28]

QoL assessments

Patients responding to tisagenlecleucel had clinically meaningful improvements in HRQoL, as assessed by both instruments (FACT-Lym and SF-36) and across subscales up to 18 months. QoL assessments were completed by 108 of 115 (94%) infused patients at baseline (screening phase), which included 57 of 60 patients who achieved a best response of CR or PR. Among the patients with CR or PR who completed a baseline assessment, 30 and 21 patients also completed an assessment at months 12 and 18, respectively. Patient characteristics for clinical responders at baseline were similar compared with the characteristics of patients who completed assessment at months 12 and 18 (supplemental Table 1).

The FACT-Lym scores were assessed at baseline and at months 3, 6, 12, and 18, and all patients and patients who achieved CR or PR showed sustained improvement in HRQoL compared with baseline across all time points and in all FACT assessment scores (Table 2; supplemental Tables 2 and 3).[15,25,26,28] Baseline FACT-Lym mean scores were similar between the total patient population (N = 108) and those patients who achieved CR or PR (n = 57). At 18 months after baseline, the mean FACT-G TS and FACT-Lym TS scores among patients with CR or PR exceeded their respective MCID upper limit. Overall, all FACT-Lym tests (FACT-G TS, FACT-Lym S, FACT-Lym TOI, and FACT-Lym TS) had improved scores above the lower limit MCID range compared with baseline scores among clinical responders at all time points. The mean FACT-G scores among patients who achieved CR or PR showed numeric improvement compared with baseline at each assessment time point and across all domains (Figure 1).[28] The highest mean change from baseline occurred at the 18-month time point for functional, physical, and social/family FACT-G domains; the largest mean change from baseline in the emotional domain was reported at month 12. The consistent improvements in mean change scores at all time points in each of the FACT-G domains aligned with an overall improvement score exceeding the lower limit of the MCID range observed in the FACT-G TS compared with baseline (Table 2).[15,25,26,28]

Among infused patients who achieved CR or PR (n = 57), SF-36 subscale scores surpassed the MCID at months 3, 6, 12, and 18 for general health, vitality, physical functioning, role-physical, and social functioning (Figure 2; supplemental Table 4). In contrast, for month 3, all patients, clinical responders, and nonresponders surpassed MCID for general health (supplemental Table 5). The SF-36 mental health subscale demonstrated numeric improvement in the mean changes from baseline at months 3, 6, and 12, but did not exceed the MCID. The bodily pain subscale showed clinically meaningful improvements over baseline at 3, 6, and 18 months. The overall physical health total score demonstrated an improved mean change from baseline above MCID at months 3, 6, and 18 (Figure 2).[28] Overall, the SF-36 subscales showed a positive mean change, and most were above the MCID and associated with meaningful improvements in HRQoL.

Assessment of patient-reported outcome completion

Most of the patient-reported HRQoL assessments were completed by clinical responders (CR and PR), and very few clinical nonresponders completed the serial HRQoL assessments because patients succumbed to their disease or withdrew from the study to pursue alternative therapies. For instance, only 9 clinical nonresponders completed the questionnaires for the FACT-Lym S assessment at month 3, and none of the clinical nonresponders completed the questionnaire during subsequent visits at months 6, 12, and 18. Overall, the rates of questionnaire completion, including both clinical nonresponders and responders, were 94% (108 of 115) at baseline, 76% (47 of 62) at month 3, 81% (35 of 43) at month 6, 86% (31 of 36) at month 12, and 65% (22 of 34) at month 18. Altogether, ~80% of patients completed the HRQoL questionnaires before month 12. The most recorded reasons for not completing the questionnaires were disease progression and death. Among the 115 patients infused, disease progression occurred in 65 (56.5%) patients, 44 of

Table 1. Patient demographics and baseline disease characteristics

Baseline characteristics	Patients (N = 115)*	Patients with CR or PR (n = 57)†	Nonresponders (n = 51)†
Age, median (range), y	56 (22-76)	58 (26-76)	50 (22-70)
Age ≥65 y, %	23	28	18
ECOG performance status 0/1, %	57/44	58/42	57/43
Central histology review, %			
Diffuse large B-cell lymphoma,	80	74	86
Transformed follicular lymphoma,	18	25	12
Double/triple hits in *c-MYC/BCL2/BCL6* genes, %	17‡	14§	24‖
Cell of origin: germinal/nongerminal center B-cell type, %¶	55/43	51/44	59/41
2/3/4-6 prior lines of antineoplastic therapy, %	44/31/20	40/35/18	51/24/24
IPI ≥ 2 at study entry, %	73	68	78
Refractory/relapsed to last therapy, %	54/46	46/54	63/37
Prior ASCT, %	49	54	43

ECOG, Eastern Cooperative Oncology Group; IPI, International Prognostic index.
*Patients infused with tisagenlecleucel.
†Patients who completed the PRO assessments at baseline.
‡c-*MYC* + *BCL2*, n = 10; c-*MYC* + *BCL2* + BCL6, n = 5; c-*MYC* + *BCL6*, n = 5.
§c-*MYC* + *BCL2*, n = 3; c-*MYC* + *BCL2* + BCL6, n = 4; c-*MYC* + *BCL6*, n = 1.
‖c-*MYC* + *BCL2*, n = 7; c-*MYC* + *BCL2* + BCL6, n = 1; c-*MYC* + *BCL6*, n = 4.
¶Determined by the Choi algorithm.
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whom died before month 12, and 12 (12.4%) of whom died by month 18.

Discussion

It is well understood that patients with DLBCL have substantially impaired HRQoL at diagnosis and after first-line treatment with currently available treatment options.[29-33] More specifically, studies of newly diagnosed patients have reported significantly impaired health and daily activity, based on HRQoL assessments.[29-31,33] After first-line treatment patient-reported HRQoL assessments have demonstrated further declines, including both physical and functional well-being outputs.[31,32] In the r/r DLBCL setting, patients were found to have the lowest HRQoL after the first treatment cycle.[34] The LY.12 clinical trial evaluated HRQoL, by using the FACT-G instrument in patients with r/r aggressive lymphomas who received second-line treatment with gemcitabine, dexamethasone, and cisplatin or dexamethasone, cytarabine, and cisplatin followed by ASCT. Overall, patients' HRQoL deteriorated from baseline, with only minimal improvement throughout the study.[35] Patients with hematologic malignancies who underwent allogenic or autologous SCT had similar HRQoL, according to the FACT-G instrument, compared with patients who underwent CAR T-cell therapy, including a short-term increase in HRQoL scores for the physical and functional well-being subgroups in patients treated with CAR T-cell therapy.[36] Currently, there are limited PRO data among patients who have received third-line treatment for r/r DLBCL, especially long-term follow-up with multiple instruments.[1] Presentations at scientific conferences showed that patients with r/r DLBCL treated with axicabtagene ciloleucel had no significant changes in mental or physical health scores from baseline to 90 days, according to SF-36 questionnaires.[37] In addition, patients with r/r DLBCL treated with lisocabtagene maraleucel demonstrated improvement of global health status, emotional, cognitive, physical, role, and social functioning within 3 months of infusion, according to the European Organization for Research and Treatment of Cancer (EORTC) questionnaire.[38] This report establishes long-term PROs for patients with r/r DLBCL and demonstrated durable and clinically

Table 2. FACT assessment scores

FACT-Lym	MCID	Baseline, mean (SD)			Change from BL month 3, mean (SD)	Change from BL month 6, mean (SD)	Change from BL month 12, mean (SD)	Change from BL month 18, mean (SD)
		All patients (N = 108)	Patients with CR/PR (n = 57)	Nonresponders (n = 51)	Patients with CR/PR (n = 39)	Patients with CR/PR (n = 34)	Patients with CR/PR (n = 30)	Patients with CR/PR (n = 21)
FACT-G TS	3-7	77.0 (16.1)	79.2 (15.2)	74.6 (17.0)	+5.8 (11.9)*	+5.8 (13.9)*	+6.3 (12.2)*	+10.0 (11.1)†
FACT-Lym S	2.9-5.4	44.4 (9.1)	45.2 (9.3)	43.6 (9.0)	+3.2 (7.4)*	+3.0 (7.7)*	+3.7 (6.5)*	+3.1 (6.6)*
FACT-Lym TOI	5.5-11	82.0 (19.0)	84.7 (18.3)	79.1 (19.5)	+5.9 (14.5)*	+6.2 (15.5)*	+6.8 (15.6)*	+9.2 (13.6)*
FACT-Lym TS	6.5-11.2	121.2 (24.0)	124.1 (22.8)	118.1 (25.1)	+9.4 (17.1)*	+8.6 (20.3)*	+9.6 (17.9)*	+13.1 (16.1)†

Plus signs (+) indicate the means reported are positive changes from baseline.[15,25,26,28]
BL, baseline. SD, standard deviation.
*The clinical meaningful improvement in HRQoL is greater than MCID lower limit.
†Clinically meaningful improvement in HRQoL is greater than MCID upper limit.

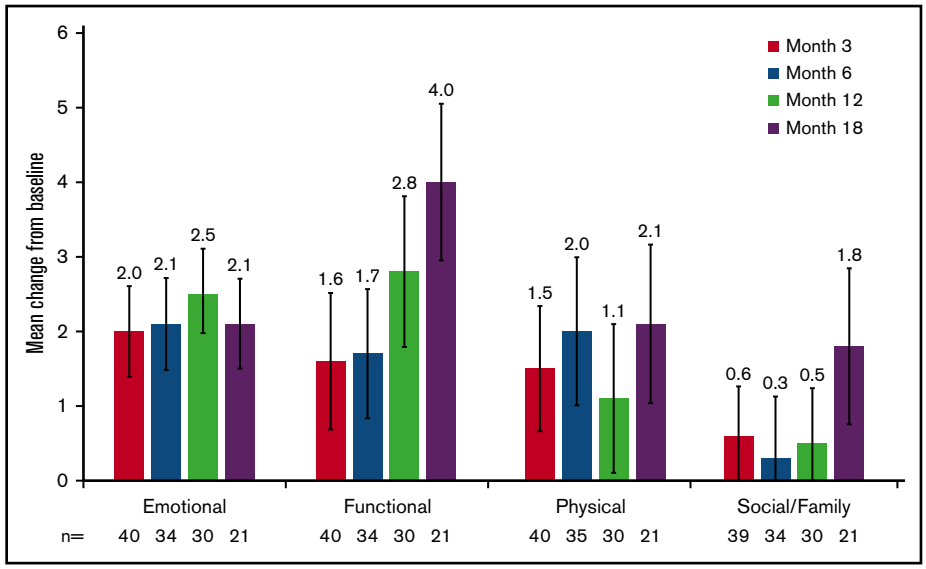

Figure 1. Mean change from baseline in FACT-G domains in patients with a CR or PR. Improved scores were observed across all categories of FACT-G assessment, which includes emotional, function, physical, and social/family categories. FACT-G, functional assessment of cancer therapy-general. Error bars represent standard error of the mean. Reproduced with permission from Tam et al.[28]

meaningful patient-reported HRQoL benefits from tisagenlecleucel therapy in the JULIET study. Improvements in HRQoL were observed across multiple subscales at the month-3 assessment and were maintained throughout month 18, and assessments are ongoing among responding patients. Scores for FACT-G, FACT-Lym, SF-36 physical component summary, and mental component summary were similar compared with NHL survivors (N = 761) at baseline[21]; however, the patients in the JULIET study demonstrated continued improvement in these scores across all assessments over time. Our results are also supported by the substantial HRQoL benefits observed with tisagenlecleucel in pediatric and young adult patients with r/r B-cell ALL who received a single infusion of tisagenlecleucel in the ELIANA study (clinialtrials.gov #NCT02435849).[39] In patients with pediatric ALL who were ≥8 years (N = 58), HRQoL was assessed using the Pediatric Quality of Life Inventory (PedsQL) and EuroQoL 5-dimension visual analog scale (EQ-5D VAS). Among clinical responders (N = 48), the mean change (standard deviation) from

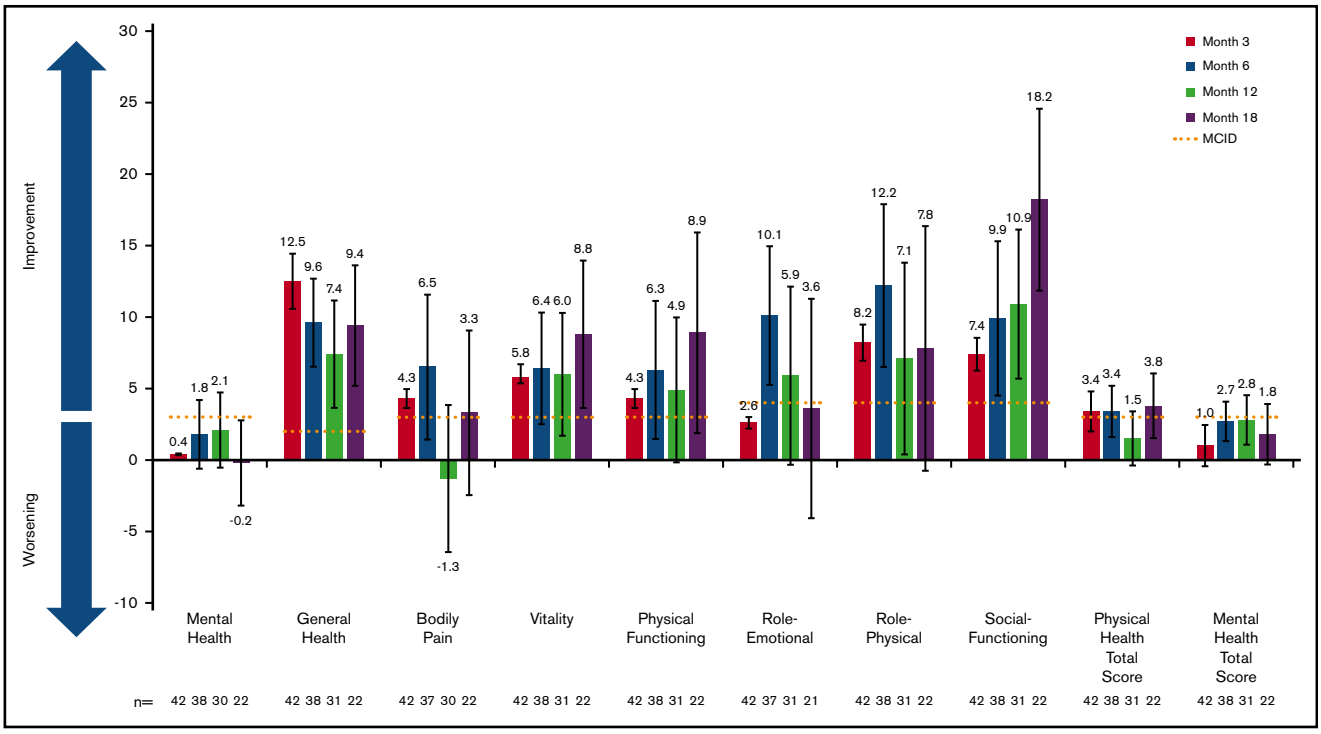

Figure 2. Mean changes from baseline in SF-36 in patients with a CR or PR. Scores above the MCID were observed in 5 of 8 subscales, which included general health, vitality, physical function, role-emotional, role-physical, and social-functioning. The total scores of physical health and mental health improved and physical health total score surpassed the MCID at month 3, 6, and 18 time points. Error bars represent standard error of the mean. Reproduced with permission from Tam et al.[28]

baseline at 12 months was 27.2 (21.7) for the PedsQL total score and 24.7 (18.6) for EQ-5D VAS. Both assessments demonstrated clinically meaningful improvements among patients who responded to tisagenlecleucel therapy.[39] Although we chose to assess HRQoL using the disease-specific instrument FACT-Lym and the more general disease instrument SF-36, other instruments such as Patient-Reported Outcomes Measurement Information System (PROMIS) will be beneficial to include in future clinical trials for CAR T-cell therapy.[40] These data, in conjunction with the results of the current study, strongly suggest that patients who respond to tisagenlecleucel therapy may produce clinically meaningful improvements in patient-reported HRQoL across at least 2 hematologic malignancies.

The JULIET study enrolled patients with r/r DLBCL who had progressive disease after ASCT or were ineligible for transplant. Most patients had received ≥2 prior lines of treatment.[10] In this r/r DLBCL patient population, there is a need for effective treatments that also improve and maintain long-term HRQoL.[34,36] Tisagenlecleucel has demonstrated a high and durable ORR with 40% of patients achieving CR, and now, durable, clinically meaningful improvements in HRQoL. The SF-36 scores reported by patients confirmed clinically meaningful improvement based on the MCID observed from months 3 through 18 for 5 of 8 subscales, including general health, vitality, physical function, role-emotional, role-physical, and social functioning. The MCIDs represent the score difference in the domain that patients perceive as important, which ultimately leads the health care provider to consider changes to the patient's management.[15,41] Therefore, approaching or surpassing the MCID for any subscale represents a clinically significant improvement in HRQoL. Overall, the physical and mental health total scores were above baseline, and the physical health total score went above the MCID for months 3, 6, and 18. In addition, FACT scores improved compared with baseline scores across the study. Two FACT scores (FACT-G TS and FACT-Lym TS at month 18) passed the upper limit of MCID, showing that those 21 patients with clinical response also had significant improvement in QoL at 18 months after infusion. All other scores passed the lower limit of MCID, showing that the improvements in QoL for clinical responders are also clinically meaningful. These positive results obtained mostly from patients responding to therapy in our study were in contrast to previous HRQoL reports for DLBCL patient populations[29,34] and underscore the clinical benefit that can be derived from a novel therapy that was highly effective with a manageable safety profile in patients with r/r DLBCL. The JULIET study incorporated a population of patients in need of effective treatments, and patients responded to tisagenlecleucel with meaningful clinical improvement of HRQoL based on 2 well-established instruments over a 19-month follow-up.

One limitation of the current study was that most of the HRQoL data were only available from infused patients who achieved CR or PR, and most patients who did not complete the HRQoL assessments discontinued the study or were lost to follow-up. Because of the lack of HRQoL assessments in patients who did not respond to tisagenlecleucel therapy, the analysis of HRQoL among patients who responded to tisagenlecleucel was a post hoc analysis. In addition, fewer patients with clinical response completed the HRQoL assessments at months 12 and 18. Thus, the relationship between treatment effect and HRQoL cannot be determined in this study. Therefore, it was not feasible to quantify the magnitude of improvement in PRO observed in patients who responded to tisagenlecleucel therapy vs standard salvage chemotherapy. Another limitation of our study is the lack of HRQoL data before and the first month after tisagenlecleucel infusion, a period when patients are likely to experience cytokine release syndrome or other serious adverse events that could affect short-term HRQoL.[40] However, because these acute-phase adverse events are effectively managed with current strategies, we chose to focus on the longer-term HRQoL impacts of tisagenlecleucel. Future studies will need to determine the appropriate timing of HRQoL evaluations after CAR T-cell therapies.

Furthermore, a recent analysis for patients with r/r DLBCL treated with lisocabtagene maraleucel demonstrated improvement in scores for global health status and emotional and cognitive function compared with baseline from months 1 to 3 after infusion, whereas physical, role, and social-functioning scores declined at month 1, followed by improvements in the following months.[38] These data suggest that CAR T-cell therapies can also affect short-term HRQoL immediately after infusion, which may lead to longer-term improvements in HRQoL as we have reported in our analysis. As ongoing CAR T-cell therapy trials are completed, these results may help to provide insight on the use and timing of PRO questionnaires in future clinical research of CAR T-cell therapies. Despite these limitations, the study establishes long-term results for HRQoL for heavily pretreated adult patients with r/r DLBCL receiving third-line treatment, importantly highlighting the promising patient benefits. Such HRQoL benefits are an important adjunct to our previous report of durable efficacy and will aid in making the decision to pursue CAR T-cell therapy in DLBCL.[10]

In summary, long-term follow-up in the phase 2 JULIET study demonstrated that adult patients with r/r DLBCL who responded to tisagenlecleucel therapy experienced a durable improvement in HRQoL. These data, together with the durable complete responses and OS benefit,[10] suggest that tisagenlecleucel improves HRQoL in patients with r/r DLBCL who respond to this therapy. This report will serve as a benchmark for understanding the HRQoL benefits of future novel treatments in r/r DLBCL and will also serve as a new baseline for comparison and evaluation of alternate CD19-targeted CAR T-cell therapies.

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Authorship

Contribution: Novartis Pharmaceutical Corporation designed the study; R.T.M., E.K.W., U.J., J.M., I.F., H.H., S.J., S.J.S., M.R.B., J.R.W., S.M., T.T., V.B., S.R.F., P.B., G.A.S., and C.S.T. enrolled patients, performed research, and contributed to data collection and interpretation; R.T.M., J.Z., R.T., L.B.P., and Q.M. performed quality of life analyses and/or statistical analyses and/or contributed to data interpretation; R.T.M., E.K.W., and C.S.T. wrote the first draft; and all

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M.R.B. is employed at United Healthcare and has provided consultancy to and held membership on the board of directors or advisory committees for Seattle Genetics; received honoraria from and participated in the speakers bureau at Celgene; and participated in the speakers bureaus at Juneau Therapeutics and Novartis. J.R.W. has held membership on the board of directors or advisory committees for Novartis, Apotex, Kite Pharma, and Celgene. S.M. has provided consultancy to and received honoraria (personal) from Novartis; received honoraria (via institution) from and participated in the speakers bureau at Celgene; held membership on and is head of the data safety monitoring board at, participated in the speakers bureau at, and received honoraria (via institution) from Miltenyi; participated in the speakers bureau at and received honoraria (via institution) from Kiadis; is part of an expert panel at and received honorarium (via institution) from Bellicum; and received honoraria (via institution) from and participated in the speakers bureau at Gilead. T.T. has provided consultancy to, received honoraria from, and held membership on the board of directors or advisory committees for Novartis; provided consultancy to, held membership on the board of directors or advisory committees for, and received research funding from Takeda and Kyowa-Hakko Kirin; provided consultancy to and received honoraria from MSD; received honoraria and research funding from Bristol-Myers Squibb and Chugai; and received honoraria from Pfizer and Celgene. V.B. has held membership on the board of directors or advisory committees for Kite Pharma, and received research funding from GT Biopharma and Gamida Cell. S.R.F. has provided consultancy to and received honoraria and travel expenses from Novartis; received honoraria from and participated in the speakers bureau at Celgene; received honoraria from Amgen; participated in the speakers bureau at Janssen; and received travel expenses from Jazz Pharma. P.B. has provided consultancy to and received honoraria from Novartis. G.A.S. has provided consultancy to and received honoraria from Novartis; received honoraria from, held membership on an advisory board for, and received research funding from Celgene; received honoraria from AbbVie, Acerta, Amgen, Epizyme, Merck, Morphosys, Pfizer, Takeda, and Servier; and received honoraria from and help membership on advisory boards for Gilead, Janssen, and Servier. J.Z., R.T., L.D.P., and Q.M. are employed at Novartis. C.S.T. has received honoraria and research funding from AbbVie, Janssen, and Beigene.

ORCID profiles: E.K.W., 0000-0003-0816-6729; U.J., 0000-0001-9826-1062; J.M., 0000-0002-0539-4796; H.H., 0000-0001-9799-9428; S.J., 0000-0002-4335-2554; J.R.W., 0000-0002-1824-2337; S.M., 0000-0002-8325-9215; T.T., 0000-0002-0941-271X; G.A.S., 0000-0002-9541-8666; L.B.P., 0000-0002-7803-2366.

Correspondence: Richard T. Maziarz, Knight Cancer Institute, Mail code OC14HO, Oregon Health and Science University, 3181 SW Sam Jackson Park Rd, Portland, OR 97239; maziarzr@ohsu.edu.

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