

Patient Perceptions Regarding Ciltacabtagene Autoleucl Treatment: Qualitative Evidence From Interviews With Patients With Relapsed/Refractory Multiple Myeloma in the CARTITUDE-1 Study

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Abstract

Ciltacabtagene autoleucl (cilta-cel) is a CAR-T cell therapy that has shown efficacy in patients with relapsed/refractory multiple myeloma, as well as improvements in health-related quality of life. Here, we capture patient perspectives on treatment with cilta-cel to provide additional context to previously reported clinical outcomes. Qualitative interviews from 36 patients showed cilta-cel met or exceeded treatment expectations.

Introduction: Ciltacabtagene autoleucl (cilta-cel), a novel chimeric antigen receptor T (CAR-T) cell therapy, has demonstrated early, deep, and durable clinical responses in heavily pretreated patients with relapsed/refractory multiple myeloma (RRMM), and improvements in health-related quality of life (HRQoL) in CARTITUDE-1 (NCT03548207). Patient perspectives on treatment provide context to efficacy outcomes and are an important aspect of therapeutic evaluation. **Methods:** Qualitative interviews were conducted in a subset of CARTITUDE-1 patients (n = 36) at screening, Day 100, and Day 184 post cilta-cel on living with MM, therapy expectations, and treatment experiences during the study. **Results:** Patients most wanted to see change in symptoms with the greatest impact on HRQoL: pain (85.2%) and fatigue (74.1%). The primary treatment expectation was achieving remission (40.7%), followed by extended life expectancy (14.8%). Patients most often defined meaningful change as improvement in symptoms (70.4%) and return to normalcy (40.7%). The percentage of patients reporting symptoms (pain, fatigue, bone fracture, gastrointestinal, neuropathy, and weakness) decreased from 85.2% to 22.2% across symptom types at baseline to 29.2% to 0% on Day 184 after cilta-cel. Improved symptoms and positive sentiments corresponded with improved perception of overall health status and reduced pain level, respectively. Most patients reported that their expectations of cilta-cel treatment had been met (70.8%) or exceeded (20.8%) at Day 184, and 70.8% of patients considered cilta-cel therapy better than

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their previous treatments. **Conclusion:** Overall HRQoL improvements and qualitative interviews showed cilta-cel met patient expectations of treatment and suggest the long treatment-free period also contributed to positive sentiments.

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Introduction

Multiple myeloma (MM) is an incurable cancer accounting for 1% of all cancers^{1,2} and is the second most common hematological malignancy.³ Patients with MM are typically treated with autologous stem cell transplant, immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs), and/or anti-CD38 antibodies, but they eventually relapse and become refractory to these therapies.^{4,5} With each successive line of therapy, the disease becomes more resistant, time to progression shortens,^{6–8} and health-related quality of life (HRQoL) declines.^{8,9} Significant levels of anxiety, depression, and psychosocial stress,¹⁰ along with disease symptoms and treatment side effects, negatively contribute to patients' daily experiences. There is a need for novel and effective therapeutics, with a key treatment goal of improving patient HRQoL.^{2,11} Patients' expectations of treatment before and during the treatment process affect their HRQoL¹² and can provide context to their perceptions of treatment outcomes. Therefore, gaining insight into patients' perspectives on their disease, treatment expectations, and treatment outcomes is an important part of evaluating new therapeutics.¹³

Cilta-cel is a chimeric antigen receptor T (CAR-T)–cell therapy with 2 B-cell maturation antigen (BCMA)–targeting single-domain antibodies. It was recently approved by the US Food and Drug Administration for the treatment of adult patients with relapsed/refractory MM (RRMM) after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody.¹⁴ CARTITUDE-1 (NCT03548207) was a phase 1b/2 study that evaluated the safety and efficacy of cilta-cel, a CAR-T cell therapy, in patients with RRMM. A single infusion of cilta-cel has shown early, deep, and durable responses in heavily pretreated¹⁵ patients with RRMM as well as clinically meaningful improvements in HRQoL.¹⁶ An exploratory objective of CARTITUDE-1 was to describe patients' pretreatment goals and expectations and posttreatment experiences with cilta-cel using qualitative interviews. In this report, we describe these patients' experiences living with MM, expectations for MM treatment, impressions of cilta-cel treatment, and how they describe meaningful change in relation to treatment.

Methods

Study Design and Patients

CARTITUDE-1 was an open-label, multicenter, phase 1b/2 study at 16 sites in the United States (US), with an additional cohort in Japan. Eligible patients had been diagnosed with MM according to International Myeloma Working Group criteria,¹⁷ had measurable disease at screening, and had an Eastern Cooperative Oncology Group performance status grade of 0 or 1. Patients had received at least 3 prior lines of MM therapy or were double refractory to

an IMiD and a PI, and had received a PI, IMiD, and anti-CD38 antibodies. Patients had documented disease progression at or before 12 months post last line of therapy.

Patients who were enrolled in the phase 2 portion of the study had the option to take part in qualitative interviews, if they were able to speak and comprehend an interview conducted in either English or Spanish and gave consent to an audio recording and release of contact details for scheduling interviews. Study coordinators introduced the qualitative interview as an optional component of the CARTITUDE-1 study during the study consenting process. Of those who consented to participate in the qualitative interview, patients were not included in the analysis if they discontinued from the CARTITUDE-1 trial, failed clinical trial screening, or withdrew consent for the qualitative interview. Patients who consented to the qualitative interview but were non-responsive to research team attempts to schedule were considered lost to follow-up for that interview but were eligible for subsequent interviews.

CARTITUDE-1 was conducted according to the principles in the Declaration of Helsinki and the International Conference on Harmonisation Good Clinical Practice guidelines. Each study center had an independent ethics committee/institutional review board to approve the study protocol. All patients provided informed consent. One of RTI International's 3 institutional review boards reviewed and granted approval of the qualitative portion of the study.

Interview Procedure

Semi-structured interviews were conducted via telephone by interviewers from AplusA (a third-party organization that specializes in patient interviews) and facilitated using 1 of 3 guides. Interviews were anticipated to last up to 30 minutes and were conducted either post screening and prior to treatment (pretreatment) or prior to screening (Interview 1) and on Days 100 (Interview 2) and 184 (Interview 3) post cilta-cel treatment. Interviews were conducted within 30 days of the appropriate clinical visit, with 12 interviews occurring beyond this 30-day window. All interviews were audio-recorded, and transcripts were produced. During the first interview prior to screening, patients were asked open-ended questions about their experience living with MM (including symptoms, daily life, and emotional impact) as well as their expectations for cilta-cel treatment. During the second and third interviews, patients were asked about any changes to their MM symptoms, impacts on daily life since study enrollment, experiences and opinions of cilta-cel treatment, and if pretreatment expectations had been met. Patients were also asked to provide 3 words to reflect how they were feeling on the day of the interview. These words were grouped into those conveying "positive" or "negative" sentiments.

Interview Analysis

Interviews were analyzed from standardized, quality-controlled transcripts using standard qualitative analysis methods to identify emerging trends from interview data. To facilitate analysis, a coding frame was developed and applied to the data by assigning codes to segments of text in the interview transcripts. Saturation was tracked and documented on a saturation grid. The coding frame was modified as the analysis progressed to accommodate information arising from the interview data. This process was conducted using qualitative analysis coding software (ATLAS.ti 7.5.18, Scientific Development, Berlin, Germany). The primary analysis was cross-sectional, and when possible, specific themes were analyzed longitudinally at the patient level.

Secondary analysis included cross-sectional and longitudinal analyses, and then themes of interest were compared with data that were collected from the Patient Global Impression of Change (PGIC) and the Patient Global Impression of Severity (PGIS). The PGIS assessed severity of patients' current pain on a 5-point verbal rating scale, and the PGIC captured patients' perceived change in their overall health status using a 7-point verbal rating scale. The PGIS was administered during the clinical visits that coincided with all 3 interviews; however, because the PGIC is contingent upon patients' recall of their overall health status compared with prior cilta-cel infusion, it was administered only on Day 100 post infusion to prevent recall inaccuracy.

Role of the Funding Source

The study sponsor, in collaboration with the authors, designed the trial, collected, analyzed, and interpreted the data, and prepared the report.

Results

Participants

Between July 26, 2019 and June 5, 2020, a total of 36 patients across 11 clinical sites in the US completed at least 1 interview. A total of 74 interviews were completed; 27 patients completed interview 1 (pretreatment), 23 completed interview 2 (Day 100), and 24 completed interview 3 (Day 184). Twenty-four patients completed ≥ 2 interviews; 14 of them completed all 3 interviews. Each interview consisted of approximately 10 questions. Interviewees had a median age of 62.5 years (range 46-77) and 55.6% were male (Supplemental Table 1). Almost all patients completed the interviews in English ($n = 34$, 94.4%); 2 patients completed their interviews in Spanish. This subset of patients had similar demographic and disease characteristics as the overall population of CARTITUDE-1.¹⁸

Before Treatment: Symptoms and Treatment Expectations

During interview 1, patients discussed a wide range of symptoms (Table 1). The most frequently reported symptoms were pain (85.2%) and fatigue (74.1%); these were also the most frequently reported as having the greatest impact on patients' lives and the symptoms they would most like to see improved.

MM also had a significant impact on patients' HRQoL, with many commenting on how it limited their ability to live a normal life (Table 2). Patients reported impact on their relationships,

psychological and emotional well-being, and social functioning. They struggled to maintain a positive mindset, felt anxious and stressed due to uncertainty surrounding treatment effectiveness and logistics, and struggled with opening up to others because they felt that their experiences would not be understood. Patients reported frequently missing social events due to MM symptoms and having to plan social activities around treatment. The burden of regular treatments and an immunocompromised state prevented engagement in social events and other daily activities outside the home (eg, shopping) due to fear of contracting an infection. Additionally, patients struggled with housework and shopping due to fatigue and pain.

Patients were worried about these limitations as well as lack of treatment effectiveness and the finite future treatment options currently available. Patients described feeling anxious and depressed. Concept saturation was high for symptom experience and HRQoL impacts; concepts of pain, fatigue, activities of daily living, social functioning, and work were selected by 63% to 85% of patients.

Generally, patients were well educated on CAR-T therapy and regarded it positively. Two patients expressed concern or worry about undergoing cilta-cel therapy; 1 was concerned about possible strong side effects after treatment, and the other patient did not specify a concern. Achieving remission (40.7%) was the primary expectation (Figure 1A) and hope (Figure 1B) of patients. In addition, several patients hoped that cilta-cel would be a cure and would be the last treatment they would undergo.

Patients defined meaningful treatment-related change as an improvement in their MM symptoms (70%; notably fatigue and pain) and a return to perceived normalcy (40.7%) (Figure 1C). For patients, a normal life was absent of symptom-related functional impairment, a compromised immune system, and the burden of continuous treatments.

After Treatment: Changes in Symptoms and HRQoL

After cilta-cel treatment, the percentage of patients reporting symptoms decreased (Figure 2). Most symptoms continued to decrease from Day 100 to Day 184. When asked about HRQoL, the most frequent areas of improvement were related to physical functioning, activities of daily life, and emotional/psychological functioning (Figure 3A, Table 3). Relationships and social functioning had less marked improvement, with roughly one-third of patients reporting no change. Across all domains, the proportion of patients with improvement increased from Day 100 to Day 184 (Figure 3B).

Almost all patients reported that changes in symptoms and HRQoL were extremely meaningful. Patients reported feeling more optimistic about the future, and that they were able to make life plans and live life like a "normal" person (Table 3). Patients also considered the break from continuous treatment as meaningful. In addition to fewer treatment-related symptoms while being "off treatment," patients reported the benefits of a treatment-free period as having greater independence, improved social functioning, and the opportunity to return to work.

Negative experiences of cilta-cel were due to post-infusion hospital stay, treatment side effects (fever), and pain associated with multiple bone marrow biopsies. At interview 2, an equivalent number of

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Table 1 Patient-reported Symptoms at Interview 1 (n = 27)

MM Symptoms, ^{a,b} n (%)	Symptoms Reported	Symptoms Reported as Greatest Impact on Patient Experience ^c	Symptoms Most Important to Improve ^c
Pain ^d	23 (85.2)	8 (29.6)	7 (25.9)
Fatigue	20 (74.1)	7 (25.9)	9 (33.3)
Bone fractures	9 (33.3)	0	0
Gastrointestinal issues ^e	8 (29.6)	0	1 (3.7)
Neuropathy	7 (25.9)	0	0
Weakness	6 (22.2)	1 (3.7)	1 (3.7)
Bone lesions	5 (18.5)	0 (0.0)	0 (0.0)
Cognitive dysfunction (eg, word loss, mental fatigue, brain fog)	4 (14.8)	0 (0.0)	1 (3.7)
Reduced appetite	3 (11.1)	0 (0.0)	0 (0.0)

MM = multiple myeloma.

^a Only includes symptoms reported by >2 patients

^b Some patients reported ≥1 symptom as the most important to improve and/or symptom with the biggest impact, which is reflected in the percentages

^c Some patients were unable to identify single symptoms that they considered having the greatest impact/most important to improve (instead reporting they wanted to see improvement in all symptoms), which is reflected in the percentages

^d Includes leg, back, and arm pain

^e Includes nausea, diarrhea, constipation, and gastrointestinal pain

Figure 1 Most Frequent Treatment-related (A) Patient Expectations, (B) Hopes, and (C) Considerations of Meaningful Changes Prior to Treatment With Cilta-cel.

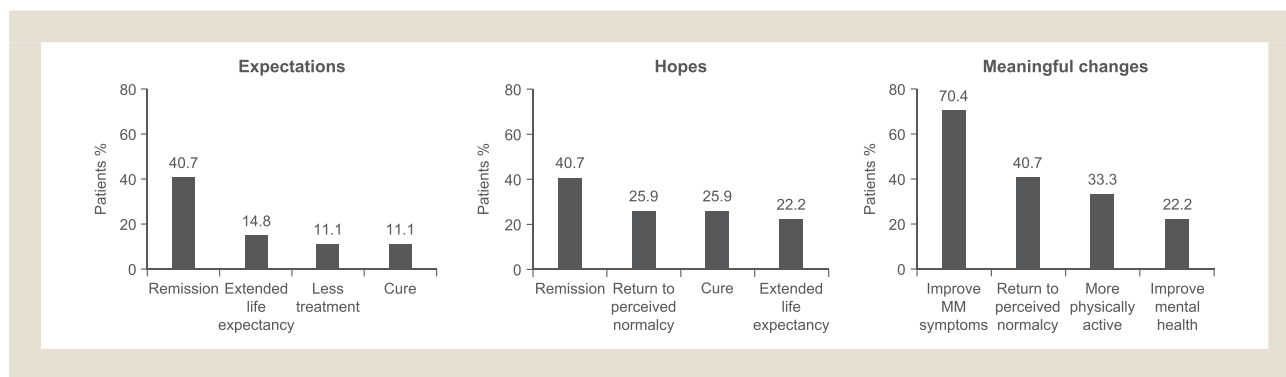


Figure 2 Symptoms Before and After Treatment With Cilta-cel. Only includes symptoms reported by >5 patients.

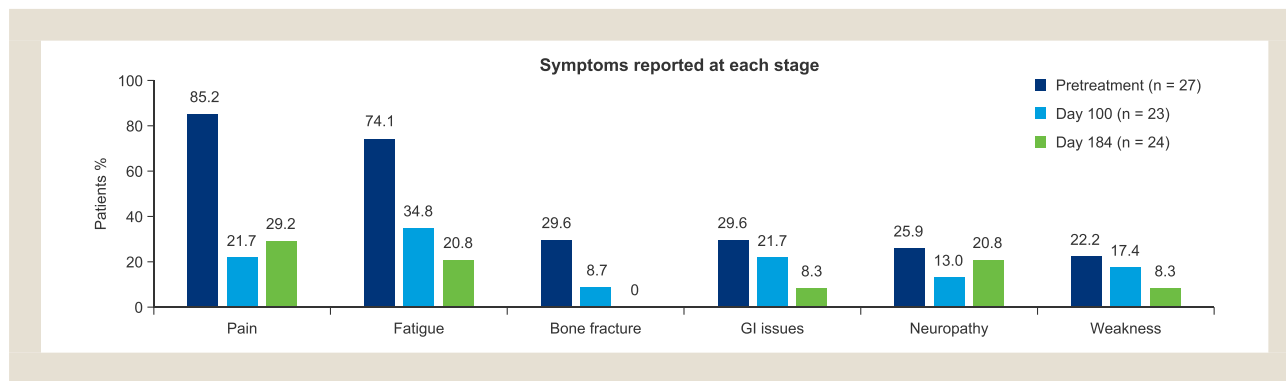


Table 2 Patient-reported HRQoL Impact of MM Reported at Interview 1

HRQoL Topic, n (%)	Pretreatment (n = 27)	Patient Experiences
Impact on relationships	25 (92.6)	"It puts me in a place where I distance myself. I distance myself from everybody, man, because don't nobody understand and there's nothing nobody can do." Male, 46 y
Psychological and emotional impact	24 (88.9)	"It's easy to make you irritable, or depressed when you have to deal with the pain everyday." Male, 62 y "...do I want to talk to some doctors or psychiatrists or something, and ... "No." They don't have multiple myeloma. They're not going to understand. I mean, they can sympathize, but they can't empathize with what I am going through." Male, 46 y "I don't know what's going to happen, so... there's a lot of anxiety. So, I would say the anxiety is the biggest problem." Female, 52 y "And there are times when I think about my own mortality maybe more than I would like to...but, generally, I'm a very optimistic person, and I don't get into these kind of funks." Female, 74 y
Activities of daily living	18 (66.7)	"I mean it's as simple as loading up the, the dishwasher, because that, I have to bend over. If I'm not holding on to nothing, it's grinding because of the, the muscles is trying to hold the, the bones is supposed to, to hold the position, so it's just constant, constant discomfort." Male, 46 y "The energy level because that... I want to be able to do things. I can handle the pain and well, the diarrhea... So, those things I can control with the medicine, but there's nothing that can give me my energy back, you know." Female, 56 y
Social functioning	17 (63.0)	"I missed out on a couple outings with my wife's family. I missed a wedding because I was sick. And I missed a class reunion because I was sick." Male, 76 y "I don't go out and do anything outside of the house much at all. I just don't want to risk getting an infection." Female, 56 y
Work	17 (63.0)	"Well, I really can't leave the house. I wouldn't be able to hold down a job, things like that." Female, 55 y "...it's the pain. It has limited me greatly... whether it's working or... spending time with my granddaughter. I'm not able to do things that I was able to do before." Male, 51 y
Exercise and sports	16 (59.3)	"I love yoga, and my friend can do yoga, and I can't. I'm going to break myself. I can't do what other people do." Female, 53 y
Physical functioning	12 (44.4)	"I can't walk very far without it hurting." Female, 67 y "I have a certain amount of neuropathy in my legs and bottom legs and hands. But it comes and goes." Male, 77 y "I do also have some intestinal problems from time to time, which I try to keep balanced." Female, 74 y "When I was first diagnosed with it, I had four fractured vertebrae in my back. That was caused from the MM." Male, 68 y
Vacations	8 (29.6)	"Well, I haven't gone on vacation, and my mom likes to travel, and my friends like to travel, and I do as well. It's very disappointing, like even a couple weeks ago, people were talking about vacations. And I'm all sad because I feel like I can't go, especially on a cruise because I can't catch like a virus, you know?" Female, 53 y
Risk aversion ^a	6 (22.2)	"You know, it's sad when you have to take a step... You can't step on a little teeny ladder to put a bulb in because you're afraid to fall, and you remember last time when you fell, it was six months before you could get chiropasty... So it's like I feel like my life is limited." Female, 53 y
Changes to diet	6 (22.2)	"...I try not to eat certain things. Like they said to me, I have to avoid sugar because the disease likes sugar." Male, 55 y
Sleep	5 (18.5)	"I mean, it's manageable and I'm able to sleep, which I wasn't before. So, I think the Vicodin has helped that, it's because I don't sleep well. I haven't for a couple of years. I get maybe three or four hours of sleep at night." Female, 67 y
Everyday travel ^b	5 (18.5)	"At this point, I'm not really driving because...of the weakness that I feel." Female, 52 y

HRQoL = health-related quality of life.

^a Includes avoiding crowds, strenuous activity.^b Includes driving, public transport.

patients used either only positive (n = 7) or only negative (n = 8) sentiment descriptors to describe their experiences with ciltacel. Eight patients reported that their treatment experiences were both positive and negative. Of the 22 patients who completed interviews 2 and 3, 10 used the same sentiment descriptors at both interviews (no change to their treatment experiences during the study), 7 patients reported a negative change from interview 2 to interview 3, and 5 reported a positive change. For patients who reported negative changes in their treatment experience, the cause was due to compli-

cations that arose from CAR-T therapy, specifically the onset of neurological side effects, gastrointestinal side effects, and hospitalization due to fever.

After Treatment: Meeting Expectations and Comparison With Previous Treatments

Most patients (>90%) reported that their expectations of ciltacel treatment had been met or exceeded (Figure 4A). Of the 3 patients who reported that their expectations had not been met (2 patients at

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Figure 3 Patient-reported Change in HRQoL Domains After Cilta-cel Treatment (A) at Day 100 and (B) at Day 184. Longitudinal analyses of patients who completed >1 interview.

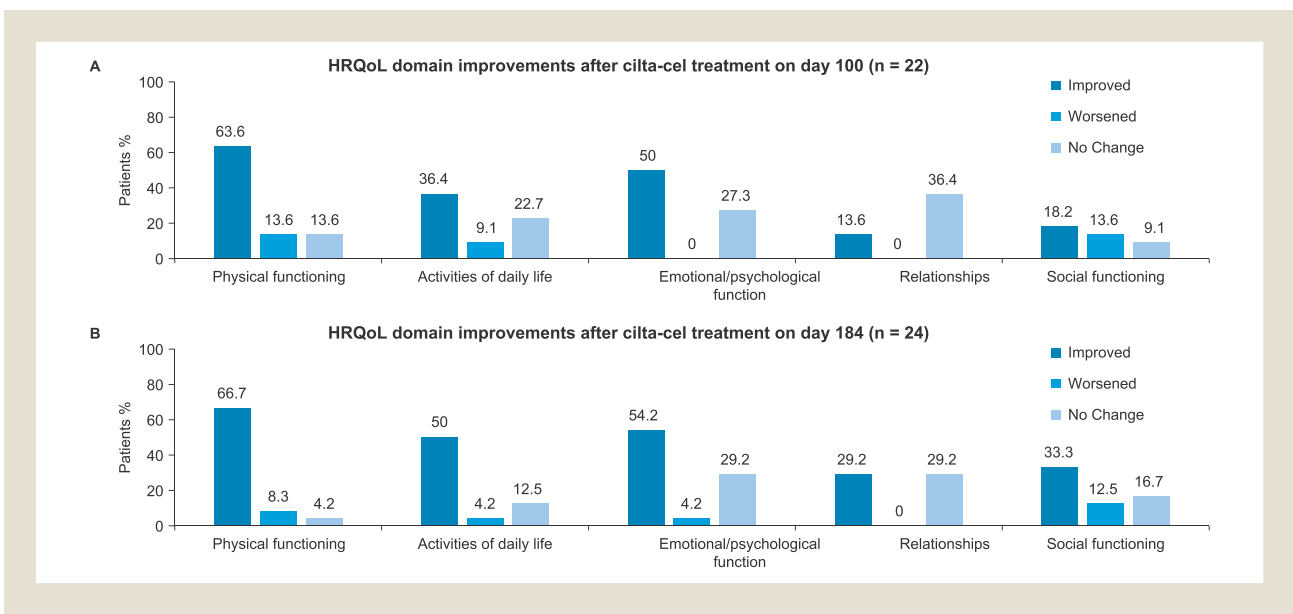


Figure 4 (A) Attainment of Cilta-cel Expectations, and (B) Comparisons With Previous Treatment. *1 patient reported that their expectations were met in terms of treatment response, but not met in terms of side effects; †1 patient was not asked whether their expectations were met. ‡Patients indicated during the interview that some aspects of cilta-cel were better than previous treatments (eg, effectiveness, administration), whereas other aspects were worse (eg, hospitalization, side effects).

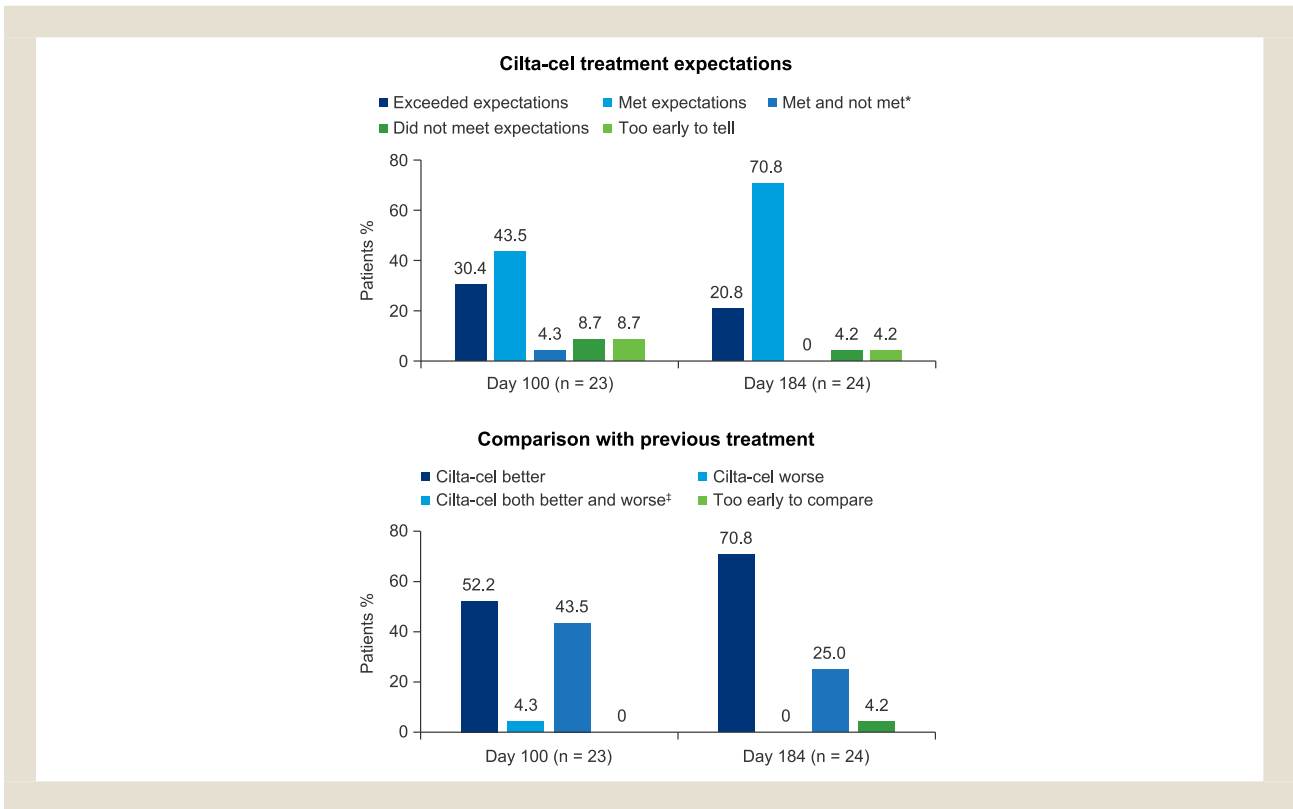


Table 3 Patient Experiences After Cilta-cel Treatment

Patient experiences regarding symptoms	<p>"Yes. I feel more energy. I feel more energy to be active... But I noticed that after the T-cell treatment, after maybe like a couple of months, my fatigue level has gone down. I'm at a... point now where I can stay up throughout the day." Male, 46 y, interview #2</p> <p>"The changes mean a lot because living in pain and being tired, or just being careful, walking gingerly, that stuff was like a new normal and it bothered me because I know within myself I wasn't like that." Male, 46 y, interview #3</p> <p>"It's just amazing to me. My neck doesn't hurt and my back. I had such back issues and that doesn't hurt anymore. So yes. It's amazing." Female, 71 y, interview #3</p>	
Patient experiences regarding HRQoL	Psychological and emotional impact	<p>"Just the positivity and knowing that things are getting better and will get better is encouraging to me." Male 67 y, interview #2</p> <p>"I feel better. So definitely change in terms of feeling better about being able to go out and enjoy, enjoy life a little more." Female, 52 y, interview #3</p> <p>"I've been dealing with the, the pain and the nausea from the chemo and stuff, and ... just six months of a break is huge." Male, 54 y, interview #3</p>
	Activities of daily living	<p>"Well, you know, like I said, I'm able to do more in terms of, if it's doing things around the house that I wasn't able to do before." Male, 67 y, interview #3</p>
	Social functioning	<p>"Well, they're very important because when you don't feel well and you've got the big cancer thing on your mind you kind of tend to... cut yourself off... You tend to withdraw. You withdraw, and I didn't want to be with anybody sometimes.. I just wanted to be alone.. It's like, I just can't get over it. I can't, I can't talk about it to people enough." Female, 71 y, interview #3</p>
	Work	<p>"It's very, very meaningful to me, and, yes, it's been amazing... And being able to go back to work is very important because, otherwise, I wouldn't be able to continue with everything that I was getting from my work. So it's like a survival saying at this point and being able to continue with my salary and health benefits and all that.." Female, 52 y, interview #3</p>
	Exercise and sports	<p>"Well, I can now do, I can exercise, I can walk, I can do all my regular activities without any problem..." Female, 77 y, interview #2</p>
	Physical functioning	<p>"Yes. I feel more energy. I feel more energy to be active... But I noticed that after the T-cell treatment, after maybe like a couple months my fatigue level has gone down. I'm at a, I'm at a point now where I can stay up throughout the day." Male, 46 y, interview #2</p> <p>"It's just amazing to me. My neck doesn't hurt and my back. I had such back issues and that doesn't hurt anymore. So yes. It's amazing." Female, 71 y, interview #3</p>
	Risk aversion	<p>"The whole COVID-19 thing I guess I would be going through all this even if I wasn't immunosuppressed, so as it turns out, in my case the timing means it's less of a problem." Male, 63 y, interview #3</p> <p>The changes mean a lot because living in pain and being tired, or just being careful, walking gingerly, that stuff was like a new normal and it bothered me because I know within myself I wasn't like that" Male, 46 y, interview #3</p>
	Everyday travel	<p>"It's given me that my own independence in a way I can go and visit whoever I need to visit and go from there. That's very important to me.." Female, 70 y, interview #3</p>
Patient experiences of cilta-cel and comparisons with previous treatments	<p>"It was pretty easy, too. Like, I was surprised at how easy it was to get the cells taken out. Get them back in and... it was just like a transfusion." Female, 56 y, interview #2</p> <p>"I got real tired of staying in the hospital for 10 days, especially after my fever broke... when I was running the fever... I guess I was happy to be there, but after the fever broke... I had nothing to do, and I wasn't really happy about being there for 10 days." Female, 66 y, interview #2</p> <p>"The only negative thing... was the fact that you have to be hospitalized for, in my case, 14 days." Male, 64 y, interview #2</p> <p>"It's a lot easier and I feel better. And I would take this any day over, like getting the chemo and all that stuff. Yes. I would definitely do this again." Female, 46 y, interview #2</p> <p>"All through treatments, chemo, I still had no energy. I wasn't getting my energy back. It was pretty much consistent, the same. That never changed, but when I had this done, the CAR T-cell, each day progressively got better." Male, 61 y, interview #3</p>	

Day 100 and 1 patient at Day 184), 2 attributed the failure to treatment side effects, and the other had anticipated feeling "normal" but this did not happen.

When patients compared their cilta-cel treatment experience with their previous treatments, they focused on specific treatment aspects rather than the overall treatment experience. Patients reported that some elements of the cilta-cel experience (eg, effectiveness, administration) were comparably better than their previous treatments, whereas other elements (eg, hospitalization, side effects) were worse than their previous treatments. By Day 184, 70.8% of patients

considered cilta-cel therapy better than their previous treatments (Figure 4B, Table 3).

Cross-sectional Analysis Comparing Qualitative Interviews With Patient-assessed Pain and Overall Change in Health Status

At interview 1 (n = 24 with available interview and PGIS data), positive and negative patient sentiments were distributed across PGIS scores (Supplemental Figure 1A). However, at interviews 2

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($n = 19$) and 3 ($n = 21$), an increase in positive sentiments corresponded with patients reporting less severe pain.

At Day 100, most patients reported better overall health status compared with pre cilta-cel treatment as measured by the PGIC. In general, improvement in symptoms tended to correspond with improved PGIC scores. When patients showed improvements in fatigue and pain, they also reported either “feeling a lot better now” or “moderately better now” on the PGIC (Supplemental Figure 1B). Improved overall health status also corresponded with treatment expectations being met or exceeded (data not shown).

Discussion

The qualitative interviews provided valuable information regarding patients’ experiences of living with MM and undergoing cilta-cel therapy. Prior to treatment, patients reported high symptom burden and detriments to HRQoL, a finding consistent with previous studies.^{6,19-22} Pain and fatigue had the most impact on patients’ lives and were considered the most important to improve. In previous qualitative studies,^{7,23} patients stressed the importance of improved HRQoL as a treatment goal; these studies concurred that pain and fatigue were primary factors affecting HRQoL.

MM had detrimental effects on patients’ abilities to perform daily activities, prevented engagement in social activities with family and friends, and impeded their ability to work, all of which likely contributed to the overwhelming emotional and psychological impact of the disease. Many of these limitations on patient activities were attributed to MM symptoms. Post cilta-cel treatment, patients reported improvement in symptoms as well as physical functioning, emotional/psychological function, and activities of daily life. For patients, symptoms and effects on HRQoL were linked; better overall health status and having positive sentiments were related to reductions in pain and fatigue. While a non-responder group was not available in the CARTITUDE-1 study, a prospective observational study of real-world clinical practice in triple-class-exposed patients (LocoMMotion) reported that gains in HRQoL were associated with depth of response.²⁴

However, most patients reported that their relationships and social functioning remained unchanged. The advanced disease status of these patients may have hindered improvement in social functioning, even though symptoms improved. Importantly, these interviews were conducted during the Coronavirus disease-2019 (COVID-19) pandemic, which likely impacted the ability to socialize through either enforced lockdown measures or self-imposed isolation to avoid contracting the virus. Even though MM-associated symptoms were alleviated with cilta-cel treatment, pandemic effects likely limited the improvements observed in relationships and social functioning.

Before treatment, most patients hoped for an improvement in MM symptoms prior to cilta-cel treatment and considered symptom improvement to be a meaningful change. Accordingly, most patients reported changes in symptoms and HRQoL that occurred after treatment as “extremely meaningful.” These were also reflected in the secondary analyses; a decrease in pain (assessed by the PGIS) led to an increase in positive sentiments, and an improvement in symptoms corresponded with better PGIC scores (a measure of overall health status).

Overall, patients reported that their expectations of treatment with cilta-cel had been met or exceeded, and that the infusion of CAR-T cells was a relatively easy process. Patients found it easier than their prior treatments and chemotherapy and expressed positive sentiments regarding the prolonged treatment-free period provided by cilta-cel. Negative experiences were associated with the post infusion hospital stay and treatment side effects. Neurological toxicities are a common complication of CAR-T therapies,²⁵ and in CARTITUDE-1, 21% of patients had CAR-T cell neurotoxicities.²⁶ For the patients who were interviewed, neuropathy, along with fever and gastrointestinal side effects, contributed to negative aspects of patient experience. Exploration of outpatient treatment in ongoing studies may improve future cilta-cel treatment experience by reducing their hospital stay.

This qualitative study has limitations. First, these interviews were optional, so not all patients who participated in CARTITUDE-1 participated in qualitative interviews. However, comparisons of these patients with the overall CARTITUDE-1 population showed that the 2 groups were similar. Additionally, concept saturation was high for symptoms and HRQoL impacts. Second, in interviews 2 and 3, patients were asked to recall their experiences when they enrolled in the CARTITUDE-1 study and compare those with previous MM treatments. This may have introduced a recall bias. Although this is a common concern for questions that target specific events, activities, or states, it diminishes when people are asked about change or progression over time. Finally, restrictions imposed during the COVID-19 pandemic may have confounded changes to patients’ HRQoL.

Conclusion

This report provides much-needed insight into patients’ expectations and experiences while undergoing CAR-T therapy. Our findings highlight the central role of pain and fatigue in driving patients’ expectations, sentiments, and perceptions of overall health status. Patients reported that cilta-cel treatment led to a decrease in symptoms, an improvement in HRQoL, a prolonged treatment-free period, and apart from posttreatment hospitalization, was a more favorable treatment process compared with other therapies. Treatment-free periods are unique to CAR-T therapies and tend to be prolonged. This benefit might have been underestimated by stopping surveys at Day 184. Continuous therapy is part of the paradigm for this patient population, and it contributes to the negative HRQoL due to frequent treatments and side effects. CAR-T therapies, such as cilta-cel, offer a unique treatment-free period, which could lead to positive impacts on patient HRQoL.

Clinical Practice Points

- Patients with MM experience periods of relapse and remission, with successively shorter periods of remission. Patients with MM also experience a reduction in HRQoL. There is a need for novel therapeutics that not only prolong patient survival, but also improve patient HRQoL. A recently approved CAR-T cell therapy – cilta-cel – has shown early, deep, and durable responses in patients with RRMM along with an improvement in patient HRQoL. Capturing patient expectations of treatment before and during a clinical trial can provide context to the trial outcomes.

- Our study showed that for patients with RRMM, symptoms of pain and fatigue had the greatest impact on HRQoL, and meaningful change included improvement of symptoms and a return to “normal life.” The percentage of patients reporting symptoms of pain and fatigue decreased post cilta-cel treatment, which led to an improved perception of overall health. The long treatment-free period after cilta-cel also contributed to positive patient sentiments. Overall, patients reported that their expectations of cilta-cel had been met or exceeded.
- Our findings provide much-needed insight into patients’ expectations and experiences when undergoing CAR-T therapies and highlight the impact of symptoms of pain and fatigue in driving patient expectations, sentiments, and perceptions of overall health. Perspectives gained from these qualitative interviews can help guide clinical decisions by adding meaningful context to trial results.

Data Sharing Statement

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at <https://www.janssen.com/clinical-trials/transparency>. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at <http://yoda.yale.edu>.

Authors’ Contributions

ADC, PH, MH, JGB, SZU, AJ, SJ, DM, YO, JDG, JMS, CCJ, SV, WD, and MA: study design, study conduct, writing – review and editing; RC, RM, and LD: conceptualization, data curation, investigation, project administration, supervision, writing – review and editing; KSG, JMF: conceptualization, supervision, writing – review and editing; KM and StS: writing – review and editing.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.cml.2022.10.001](https://doi.org/10.1016/j.cml.2022.10.001).

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