Weathering the storm when the end of the road is near: A qualitative analysis of supportive care needs during CAR T cell therapy in pediatrics

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Abstract

Background: Chimeric Antigen Receptor (CAR) T cell therapy provides promising outcomes in relapsed/refractory B Acute Lymphoblastic Leukemia (ALL) yet still carries high toxicities rates and relatively poor long-term survival. Efficacy has yet to be demonstrated in other diagnoses while toxicity and risk profiles remain formidable. To date, treatment-related symptom burden is gleaned from clinical trial toxicity reports; the patient perspective remains understudied. **Methods:** English or Spanish-speaking patients (ages 8-25 years) undergoing CAR T cell therapy for any malignancy and their primary caregiver were recruited from Seattle Children's Hospital (SCH), St. Jude Children's Research Hospital (SJCRH), and the Pediatric Oncology Branch of the National Cancer Institute (NCI). Both patient and caregiver completed semi-structured dyadic interviews 3-months post-treatment. We used directed content analysis for codebook development and thematic network analysis for inductive qualitative analysis. **Results:** Twenty families completed interviews (13 patients, 15 parents). Patients were a median age 16.5 years, predominantly female (65%), white (75%), and diagnosed with ALL (75%). Global themes included "A clear decision," "Coping with symptoms," and "Unforeseen psychosocial challenges." When families were asked to describe the "most challenging part of treatment," most described "the unknown." Most reported "the symptoms really weren't that bad," even among patients hospitalized for severe toxicity events. Fatigue, pain, and nausea were the most prevalent symptoms. Importantly, only one family would have chosen a different therapy, if given another opportunity. **Conclusions:** Although physical symptoms were largely tolerable, recognizing supportive care opportunities remains imperative, particularly psychosocial concerns.

Introduction

The modern era of cancer treatment is ripe in number and variety of therapies.[1, 2] Chimeric antigen receptor (CAR) T cell therapy is a prime example of this complex paradigmatic shift. Promising early response outcomes in acute lymphoblastic leukemia (ALL) opened the door to applying adoptive cell therapies to other malignancies and patient populations.[3-5] Despite this promise, CAR T cell therapy remains an experience of advanced cancer; CAR T cell therapy is exclusively used in advanced disease and survival after therapy for all indications remains relatively unfavorable.[6, 7]

Best practices in palliative and supportive care need to parallel this evolution in cancer care.[8-12] Decision-making becomes increasingly complex for both clinicians and families. Prognostic uncertainty, unfamiliar toxicity profiles, and the unclear significance of tumor-specific molecular profiles are now routine considerations in the family decision-making process.[13] Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), two hallmark acute toxicity events following CAR T cell therapy, are commonly encountered in the first month after therapy.[14] Symptom burden has been described as significant in adults after CAR T cell therapy, particularly those who experience CRS and ICANS.[15-17] Different from other early phase clinical trials, CAR T cell therapy clinical trials often require family relocation to one of a limited number of centers, typically for weeks of close observation for acute toxicity. However, few patient-centered supportive care recommendations exist for this population.[18] Further, supportive care needs, particularly from the perspective of the patient and family, are largely undescribed.[19-21]

The objective of this qualitative study was to understand supportive care needs during CAR T cell therapy from the perspectives of pediatric patients and their parent caregivers. We aimed to identify opportunities for improvement in symptom management, communication, and psychosocial support, with the greater goal of informing optimal supportive care management.

Methods

Design, Setting, and Participants

The "CAR T Patient Reported Outcome (PRO)" study was a prospective, mixed methods study with a primary objective to describe patient-centered outcomes in children and young adults during CAR T cell therapy. Seattle Children's Hospital (SCH), St. Jude Children's Research Hospital (SJ), and the Pediatric Oncology Branch of the National Cancer Institute (NCI) served as study sites. All sites are large referral centers for CAR T cell therapy, primarily delivered as part of clinical trials. Local IRB approval was granted at all centers in accordance with the US Federal Policy for the Protection of Human Subjects.

Recruitment took place from February 2020 through December 2022. Patient and parent caregiver ("parent") participants were recruited as dyads (patient and parent together). Enrollment of both patient and parent was not required for study participation. Patient eligibility criteria included age 8-25 years, ability to speak/read English or Spanish, and scheduled to receive CAR T cell therapy for any malignancy. Parent eligibility included being a primary caregiver of a patient aged 2-25 years undergoing treatment with CAR T cell therapy as described above and ability to speak/read English or Spanish. Exclusion criteria included lack of fluency in English or Spanish, impairment preventing interview participation, or parent refusal to allow minor participation. Study staff reviewed clinic schedules to identify eligible participants. Participants were sequentially recruited in-person before lymphodepleting chemotherapy. Per institutional standards, written informed consent (> 18 years)/written assent with parental permission (<18 years) was obtained by a trained study member. As participants approached three-months post-infusion, they were sequentially invited to participate in an optional interview. Recruitment continued until thematic saturation was achieved, determined by study team consensus.

Data Collection

Demographic and clinical data were abstracted from the patient's medical record at time of enrollment. Additional self-reported demographic data were collected from both patient and parent participants at time of enrollment via REDCap. Qualitative data collection and analysis followed the Standards for Reporting Qualitative Research guidelines.[22] Study staff trained in qualitative methods conducted interviews at their local institution (SCH: AS, KS; SJ: AK; NCI: LW). Interviews occurred between April 2020 and August 2022. The interview guide was based on models of HRQOL and symptom burden[23, 24] and informed by the research team's clinical experience. The finalized interview guide consisted of open-ended questions and optional probes to facilitate semi-structured interviews (Appendix A). The primary aim of the interview was to explore supportive care needs during CAR T cell therapy, focusing on symptom burden, communication needs/preferences, and psychosocial support. Interviews were completed by phone three months post-infusion (+/- four weeks). For families where both the child and parent participated, families chose joint or separate

interviews per personal preference. Interviews were audio-recorded, de-identified, and transcribed verbatim. The mean duration was 34 minutes (range 10-70 minutes). A $25 gift card was offered to each participant following interview completion.

Data Analysis

We used directed content analysis for codebook creation followed by in-depth thematic networks analysis to explore supportive care needs with CAR T cell therapy in pediatrics.[25-29] The multi-disciplinary analysis team included a health services investigator with qualitative research expertise (KS), physician-researchers trained in palliative care and pediatric oncology (AS, SS, DL, HS), a social work clinician-researcher (LW), and clinical research staff with qualitative research experience (KP, JN, DV). The research team used directed content analysis to guide iterative codebook development and coding structure, applying models of HRQOL and symptom burden (Appendix B).[23, 24] Starting with 5 transcripts, two coders (KS, AS) independently reviewed transcripts in their entirety and deductively applied the existing *a priori* codes for codebook refinement and addition of codes thought to be missing. Separate codes for "patient viewpoint" and "parent viewpoint" were used to organize perspectives. We continued this process until no further code categories emerged and consensus was reached.

Interviews and the finalized codebook were imported into Dedoose for analysis [Dedoose Version 7.0.23 (2016). Los Angeles, CA: SocioCultural Research Consultants, LLC www.dedoose.com]. A core of five study team members (AS, SS, KP, JN, DV) reviewed five transcripts together to establish a standard coding process. For the remaining 17 transcripts, two members of the core analysis team independently and blindly coded each transcript. A third coder reviewed each transcript, serving as a tie-breaker in code reconciliation. The core analysis team met weekly to discuss inconsistencies, resolve discrepancies, refine code definitions, and reach consensus.

After coding was complete, the full analysis team (AS, SS, KP, JN, DV, DL, HS, LW) applied thematic networks analysis to examine recurring concepts among interviews.[27] The relationship between concepts was then used to create basic themes. Basic themes were then used to create three organizing themes. Organizing themes were reorganized to deductively develop three overarching global themes representing the unique perspective of pediatric patients treated with CAR T cell therapy and their parents. Through an iterative process, the study team refined and synthesized themes within the network until inductive thematic analysis was reached.[30]

Results

Twenty families were interviewed (13 patients, 15 parents; **Table 1**), at which point we achieved thematic saturation. Of the patient interviews, six were completed with their parent, two separate from their parent, and five without a corresponding parent interview. Of the parent interviews, seven were completed without a corresponding patient interview. Ten patients were treated at SCH, six at SJ, and four at the NCI. The median age of the patient participant at time of enrollment was 16.5 years (range: 8-24). Patients predominantly identified as female (65%) and white (80%). Most patients received CAR T cell therapy for treatment of ALL (80%). The parent participant median age was 47 years (range: 31-54). Parents predominantly identified as female (93%) and white (93%). All interview participants spoke English as a primary language. Three global themes summarize the family-centered experience with CAR T cell therapy: "A clear choice," "Coping with symptoms," and "Unforeseen psychosocial challenges." (**Table 2**). Responses from the patient perspective did not significantly differ thematically from the parent perspective.

" A clear choice "

Deciding to pursue CAR T cell therapy was described as a "clear choice" by all families. Two decision-making paths were cited. Most commonly (n=13), families felt that CAR T cell therapy was unequivocally "the next best step." For most, this reflected recommendations for the best chance for cure. Other families described CAR T cell therapy as the best choice to buy time until another treatment or to extend their child's life. Alternatively, five families felt they reached the "end of a road" and were faced with no other options. One

patient explained, "It was really the only thing I had left, after 12 rounds of chemo, radiation, and a bone marrow transplant not working" (CTP041). Families also described toxicities from prior therapies leaving few other safe options, including ineligibility for otherwise standard therapies, such as stem cell transplant. One parent shared, "There's no way his body could've handled such large doses to do that again, to get him into remission, to get him to transplant. There's just no way" (CTP051P). Of the remaining two families, one chose CAR T cell therapy for quality of life and the other to avoid toxicity. Factors facilitating the family decision-making process were organized into three themes: hope, trust, and self-efficacy.

Regardless of the rationale described, expressions of hope were pervasive when families reflected upon their decision-making process. Primarily, this took the shape of optimism in CAR T cell therapy for cure. Hope for comfort and minimal toxicity was also common. For example, one parent shared, "We really want what's best for her, what was her best shot, and what will be the best way for her to be comfortable" (CTP055P). Hope for more time was also expressed. One parent explained, "That's my goal is just to keep him going as long as possible in the hope that somebody figures it out." (CTP029P).

Families expressed tremendous trust in their medical teams when reflecting on their decision-making process. Most families disclosed that they avoided the internet or social connections for information, but rather turned to their primary oncologist. One patient shared, "I mean I have all the trust in the world in my Oncology doctor, and so I told my mom from the beginning, whatever <Doctor> suggested is what I was gonna do. So I didn't really want to spend my free time looking at it <the internet>" (CTP041). Another parent expressed, "I think getting the doctor's opinion, from a doctor that knows <Child> and has been with her through her whole treatment is probably the most helpful, because I think he's got her best interest at heart." (CTP026P).

Despite expressing deep trust in their medical teams and hope for treatment success, families voiced a critical need for taking ownership in preparing themselves for treatment. This was organized into the theme "self-efficacy." Multiple families shared they felt a duty to ask questions to advocate for their child. When asked about advice for future families preparing for CAR T cell therapy, one parent offered, "Ask a lot of questions and just make sure that you're going into it as informed as you possibly can. And I think that's really served <Child> well, because we know our child better than anybody else. So just having the ability to not be afraid to ask questions and follow up with things and make sure that things aren't forgotten is really important, just to be a part of the medical team" (CTP002P).

Regardless of the decision-making mechanism, all but one family reported being satisfied with their decision and would make the same choice again. Notably, none of the families interviewed had a child who died before the interview. The sole family expressing decision dissatisfaction experienced a severe adverse event from treatment.

" Coping with symptoms"

The three most prevalent symptoms included pain, fatigue, and nausea. Overwhelmingly, families reported that physical symptoms during CAR T cell therapy were tolerable. Families were struck by this "feeling normal," both physically and as a reflection of life returning to ordinary. This sentiment was organized into the theme "Normalcy." Multiple patient participants noted a resolution of baseline physical symptoms, such as pain or nausea, and gaining a sense of independence, with n=4 participants using the word "normal." One participant shared, "I really enjoyed being somewhat independent, a little bit, considering the past four years I've kind of been pretty dependent on my parents and caregivers" (CTP017). This participant then described being able to resume college classes in the time since their infusion. Another parent reflected, "Its been really nice to be able to be at home and to kind of feel like we are living a somewhat normal life because he feels probably better than he can remember feeling... He just feels well. He feels like a normal little boy" (CTP015P).

Most of the symptoms were attributed to lymphodepleting chemotherapy. Symptoms from CRS and ICANS were infrequently discussed, including among patients with reported severe toxicity. Symptoms were often compared to experiences with prior therapies, including intensive chemotherapy or hematopoietic stem cell

transplant, reporting that symptoms experienced with these prior therapies were more significant than those experienced with CAR T cells. To reflect this viewpoint, we organized this experience into the theme "Perspective."

Finally, families acknowledged grappling with a "symptom paradox," a counterintuitive desire for symptoms to occur with therapy, attributing the presence of symptoms to be a sign of efficacy. One family explained: "Strangely enough, it made us sort of feel comforted when he did spike a high fever because it made us think that maybe it was working, 'cause that's what we were told beforehand... It might not happen, but if it does happen, that could be a good indication that it's working.' So as soon as it did happen and he spiked a fever, my husband was inpatient with him and he called me and he was like 'He spiked a fever!' and we both (it was weird) got a little bit excited like 'Okay, this is good!"' (CTP015P).

" Unforeseen psychosocial challenges "

Challenges of CAR T cell therapy were organized into three themes. First, families reflected on the emotional and financial sacrifices of being away from home, organized into the theme "The toll of being away from home." Many families relocated for treatment, requiring the family to live local to the treating center for weeks. Although families acknowledged the benefits of technology for staying connected, they lamented the physical separation. One parent shared, "You just don't see the people you're used to seeing every day. She made a lot of new friends and with video chat, life has turned out to be a whole lot different, but it's still hard to not sit and watch movies together, or eat dinner together as a family, or call her brothers to come over and visit. You have to call them on video chat. It wasn't awful; it was just different" (CTP066P). Other families described the financial costs of transportation or lodging. For example, one family shared, "I mean it's a financial strain. Things work out. You give-and-take in different places, but just being that far away from home is costly" (CTP020P).

The second challenge described was navigating unexpected scenarios, organized into the theme "The unexpected." Predominantly this related to development of toxicity, requiring longer than expected hospitalizations or changes in subsequent therapy. One parent shared, "The last thing I would expect is that the clinical trial would then cause a reason to not get treatment after that. I mean and in <Patient's> case, she's had a lot of progression since then, so I can't blame anyone and I don't have a magic ball, but it does make us wonder like if we didn't have that issue and we were able to get her on another treatment after the trial, would she have this level of progression since the trial" (CTP028P).

Finally, families endorsed the challenges of navigating novel therapies, organized into the theme "The unfamiliar." One family explained, "I feel like if it was farther along in the CAR T development and research and knowledge, that maybe they could've ironed out a few more kinks and understand more about how it works and why it works... and maybe we could've had more options about which kinds of CAR Ts we could've done here, and maybe we would've had better results and been able to get straight to transplant, but it is what it is and we are where we are" (CTP047).

Discussion

This qualitative study seeks to describe supportive care needs during CAR T cell therapy from the child and parent perspectives. Among families who chose to proceed with CAR T cell therapy, we found most families felt this was a clear decision. Symptoms were tolerable and some families reported a "symptom paradox," a desire for some toxicity to feel like the treatment was working. Families described feeling challenged by the emotional and financial burdens of relocating and the unpredictability of navigating a novel therapy. Altogether, these insights highlight opportunities for future supportive care intervention.

Families predominantly felt the path to their decision was straightforward. Hope, trust, and self-efficacy facilitated the decision-making process. Qualitative decision satisfaction was prevalent in our sample, with all but one family disclosing they would make the same decision again. Confirmation bias may partly explain this degree of decision satisfaction, as described in another general pediatric oncology study.[31] Prevalence of hopeful patterns of thought, trust in the medical team, and perceived self-efficacy were previously described

as protective against regret,[31-34] which may also be the case in our sample. Moreover, these constructs are important mitigators of uncertainty-related distress, a source of emotional distress common not only to our pediatric cohort, but another study among adult patients treated with CAR T cell therapy.[21, 35] Thus, supporting hope, trust, and self-efficacy are likely important in providing quality supportive care for families during CAR T cell therapy. General psychosocial challenges, though not unique to CAR T cell therapy, were also commonly endorsed in our study. Altogether, our findings reinforce the importance of a multidisciplinary team to support families through the challenges of therapy.[18]

Although families generally reported tolerable symptoms, our themes expose risks of inadequate symptom management. Experiential knowledge undoubtedly produced a response shift affecting families' perception of symptom burden during therapy.[36] Symptom normalization results in the perception, in both clinicians and families, that symptom-related suffering is a "normal" part of treatment and that adequate symptom control is unattainable.[37] For example, when families accept nausea and vomiting to be a "normal" part of chemotherapy, they may be less likely to request support in symptom management. Specific to CAR T cell therapy, normalizing the experience of CRS and ICANS may lead families to consider symptom management unnecessary. Further, when early toxicity with CAR T cell therapy is considered an indication of efficacy,[38]symptoms become a welcomed experience, resulting in a so-called "symptom paradox" effect. Uncertainty-related distress may develop in anticipation of CRS or ICANS. Altogether, this represents an opportunity for improving family support through both the language we use when counseling for treatment and the screening of symptoms during treatment.

Our sampling procedures were limited by interviewing families who chose and successfully completed treatment with CAR T cell therapy. Thus, the full spectrum of decision-making is not represented. Importantly, the rationale and needs probably differ between families that choose CAR T cell therapy and those who do not. Further, our study does not represent the experience of families with prohibitive access to such investigative therapy. The families in our study emphatically articulated the importance of self-efficacy in accessing CAR T cell therapy and in adequately preparing themselves for the medical and emotional complexities of treatment. Paired with the deep sense of trust our participants shared with their medical team, this poses a serious threat among disenfranchised people to access CAR T cell therapy.[39] Racial, ethnic, and payor disparities exist in referral practices for CAR T cell therapy and inclusion in clinical trials.[40] Identifying interventions to mitigate these risks must be a priority for future investigation.

Several additional limitations of this study must also be noted. Despite recruiting Spanish-speaking participants, only English-speaking participants volunteered for interview participation. Thus, our findings likely do not represent the experience of non-English speaking families. Only one father was represented in the parent participants. Our participants described predominantly positive experiences. This may reflect social desirability bias or recall bias. We chose to interview patients receiving CAR T cell therapy for any malignancy type; we continued data collection until thematic saturation was achieved and thematic differences were not appreciated between diagnosis groups. Finally, because memory impairment and severe illness are common with CAR T cell therapy, we chose to interview parents and their children together to capture a cohesive narrative. This approach may limit participant disclosure from both the parent and child perspectives. However, we did not appreciate a difference in themes between those interviewed alone and those interviewed together. Despite these limitations, our findings expose opportunities for possible intervention and priorities for future investigation.

Children undergoing CAR T cell therapy and their families, like families pursuing other advanced cancer therapies, are at risk for distress from decision making, symptoms, and uncertainty. Supportive care practices that minimize the impact of these risk factors and support hope, trust, and self-efficacy are opportunities to improve clinical care and patient and parent quality of life.

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References:

1. Butler E, Ludwig K, Pacenta HL, Klesse LJ, Watt TC, Laetsch TW. Recent progress in the treatment of cancer in children. *CA Cancer J Clin* . Jul 2021;71(4):315-332. doi:10.3322/caac.21665

2. Scott EC, Baines AC, Gong Y, et al. Trends in the approval of cancer therapies by the FDA in the twenty-first century. *Nat Rev Drug Discov* . Aug 2023;22(8):625-640. doi:10.1038/s41573-023-00723-4

3. Hunger SP, Raetz EA. How I treat relapsed acute lymphoblastic leukemia in the pediatric population. *Blood* . Oct 15 2020;136(16):1803-1812. doi:10.1182/blood.2019004043

4. Lin YJ, Mashouf LA, Lim M. CAR T Cell Therapy in Primary Brain Tumors: Current Investigations and the Future. *Frontiers in Immunology* . Feb 21 2022;13doi:ARTN 817296

10.3389/fimmu.2022.817296

5. Del Bufalo F, De Angelis B, Caruana I, et al. GD2-CART01 for Relapsed or Refractory High-Risk Neuroblastoma. *N Engl J Med* . Apr 6 2023;388(14):1284-1295. doi:10.1056/NEJMoa2210859

6. Shah NN, Lee DW, Yates B, et al. Long-Term Follow-Up of CD19-CAR T-Cell Therapy in Children and Young Adults With B-ALL. *J Clin Oncol* . May 20 2021;39(15):1650-1659. doi:10.1200/JCO.20.02262

7. Long KB, Young RM, Boesteanu AC, et al. CAR T Cell Therapy of Non-hematopoietic Malignancies: Detours on the Road to Clinical Success.*Front Immunol* . 2018;9:2740. doi:10.3389/fimmu.2018.02740

8. Webb JA, Kamal AH, LeBlanc TW. A New Frontier for Palliative Care: The Need to Train Palliative-Oncology Subspecialists. *J Palliat Med* . Dec 2018;21(12):1679-1680. doi:10.1089/jpm.2018.0421

9. Freedman JL, Beeler DM, Bowers A, et al. Supportive Care in Pediatric Oncology: Opportunities and Future Directions. *Cancers (Basel)* . Nov 23 2023;15(23)doi:10.3390/cancers15235549

10. Sampetrean A, Aldea M, Mateus C. Precision medicine's new frontier: integrating palliative care at the right time. *ESMO Open* . Oct 2023;8(5):101632. doi:10.1016/j.esmoop.2023.101632

11. Weaver MS, Heinze KE, Kelly KP, et al. Palliative Care as a Standard of Care in Pediatric Oncology. *Pediatr Blood Cancer* . Dec 2015;62 Suppl 5:S829-33. doi:10.1002/pbc.25695

12. Wiener L, Kazak AE, Noll RB, Patenaude AF, Kupst MJ. Standards for the Psychosocial Care of Children With Cancer and Their Families: An Introduction to the Special Issue. *Pediatr Blood Cancer* . Dec 2015;62 Suppl 5:S419-24. doi:10.1002/pbc.25675

13. Temel JS, Shaw AT, Greer JA. Challenge of Prognostic Uncertainty in the Modern Era of Cancer Therapeutics. *J Clin Oncol* . Oct 20 2016;34(30):3605-3608. doi:10.1200/JCO.2016.67.8573

14. Maude SL. Tisagenlecleucel in pediatric patients with acute lymphoblastic leukemia. *Clin Adv Hematol Oncol* . Oct 2018;16(10):664-666.

15. Ruark J, Mullane E, Cleary N, et al. Patient-Reported Neuropsychiatric Outcomes of Long-Term Survivors after Chimeric Antigen Receptor T Cell Therapy. *Biol Blood Marrow Transplant* . Oct 9 2019;doi:10.1016/j.bbmt.2019.09.037

16. Akinola IM, Cusatis R, Pasquini MC, et al. Multi-Stakeholder Qualitative Interviews to Inform Measurement of Patient Reported Outcomes After CAR-T. *Transplant Cell Ther* . Apr 2023;29(4):254 e1-254 e9. doi:10.1016/j.jtct.2023.01.004

17. Whisenant MS, Srour SA, Williams LA, et al. The Unique Symptom Burden of Patients Receiving CAR T-Cell Therapy. *Semin Oncol Nurs* . Dec 2021;37(6):151216. doi:10.1016/j.soncn.2021.151216

18. Steineck A, Wiener L, Mack JW, Shah NN, Summers C, Rosenberg AR. Psychosocial care for children receiving chimeric antigen receptor (CAR) T-cell therapy. *Pediatr Blood Cancer* . May 2020;67(5):e28249. doi:10.1002/pbc.28249

19. Chakraborty R, Sidana S, Shah GL, Scordo M, Hamilton BK, Majhail NS. Patient-Reported Outcomes with Chimeric Antigen Receptor T Cell Therapy: Challenges and Opportunities. *Biol Blood Marrow Transplant* . May 2019;25(5):e155-e162. doi:10.1016/j.bbmt.2018.11.025

20. Efficace F, Cannella L, Sparano F, et al. Chimeric Antigen Receptor T-cell Therapy in Hematologic Malignancies and Patient-reported Outcomes: A Scoping Review. *Hemasphere* . Dec 2022;6(12):e802. doi:10.1097/HS9.0000000000000802

21. Stenson CL, Vidrine J, Dewhurst F, Osborne W, Menne T, Stocker R. A qualitative service evaluation of patient and caregiver experiences of CAR-T therapy: Recommendations for service development and implications for palliative care teams. *Palliat Med* . Feb 2023;37(2):215-220. doi:10.1177/02692163221138880

22. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations.*Acad Med* . Sep 2014;89(9):1245-51. doi:10.1097/ACM.0000000000000388

23. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA* . Jan 4 1995;273(1):59-65.

24. Collins JJ, Byrnes ME, Dunkel IJ, et al. The measurement of symptoms in children with cancer. *J Pain Symptom Manage* . May 2000;19(5):363-77.

25. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res* . Nov 2005;15(9):1277-88. doi:10.1177/1049732305276687

26. Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study.*Nurs Health Sci* . Sep 2013;15(3):398-405. doi:10.1111/nhs.12048

27. Attride-Stirling J. Thematic Networks: an analytic tool for qualitative research. *Qualitative Research* . Dec 1, 2001 2001;1(3):385-405. doi:10.1177/146879410100100307

28. Elo S, Kyngas H. The qualitative content analysis process. *J Adv Nurs* . Apr 2008;62(1):107-15. doi:10.1111/j.1365-2648.2007.04569.x

29. Burns NaG, S.K. *The Practice of Nursing Research: Conduct, Critique and Utilization* . 5th ed. Elsevier Saunders; 2005.

30. Saunders B, Sim J, Kingstone T, et al. Saturation in qualitative research: exploring its conceptualization and operationalization.*Qual Quant* . 2018;52(4):1893-1907. doi:10.1007/s11135-017-0574-8

31. Robertson EG, Wakefield CE, Shaw J, et al. Decision-making in childhood cancer: parents' and adolescents' views and perceptions.*Support Care Cancer* . Nov 2019;27(11):4331-4340. doi:10.1007/s00520-019-04728-x

32. Sisk BA, Kang TI, Mack JW. The evolution of regret: decision-making for parents of children with cancer. *Support Care Cancer* . Mar 2020;28(3):1215-1222. doi:10.1007/s00520-019-04933-8

33. Feifer D, Broden EG, Xiong N, et al. Mixed-methods analysis of decisional regret in parents following a child's death from cancer.*Pediatr Blood Cancer* . Oct 2023;70(10):e30541. doi:10.1002/pbc.30541

34. Wakefield CE, Hetherington K, Robertson EG, et al. Hopes, concerns, satisfaction and regret in a precision medicine trial for childhood cancer: a mixed-methods study of parent and patient perspectives. *Br J Cancer* . Nov 2023;129(10):1634-1644. doi:10.1038/s41416-023-02429-1

35. Stewart JL, Mishel MH, Lynn MR, Terhorst L. Test of a conceptual model of uncertainty in children and adolescents with cancer. *Res Nurs Health* . Jun 2010;33(3):179-91. doi:10.1002/nur.20374

36. Sprangers MA. Response-shift bias: a challenge to the assessment of patients' quality of life in cancer clinical trials. *Cancer Treat Rev* . Jan 1996;22 Suppl A:55-62. doi:10.1016/s0305-7372(96)90064-x

37. Requena ML, Avery M, Feraco AM, Uzal LG, Wolfe J, Dussel V. Normalization of Symptoms in Advanced Child Cancer: The PediQUEST-Response Case Study. *J Pain Symptom Manage* . Apr 2022;63(4):548-562. doi:10.1016/j.jpainsymman.2021.12.009

38. Brammer JE, Braunstein Z, Katapadi A, et al. Early toxicity and clinical outcomes after chimeric antigen receptor T-cell (CAR-T) therapy for lymphoma. *J Immunother Cancer* . Aug 2021;9(8)doi:10.1136/jitc-2020-002303

39. Newman H, Li Y, Liu H, et al. Impact of poverty and neighborhood opportunity on outcomes for children treated with CD19-directed CAR T-cell therapy. *Blood* . Feb 9 2023;141(6):609-619. doi:10.1182/blood.2022017866

40. Hall AG, Winestone LE, Sullivan EM, et al. Access to Chimeric Antigen Receptor T Cell Clinical Trials in Underrepresented Populations: A Multicenter Cohort Study of Pediatric and Young Adult Acute Lymphobastic Leukemia Patients. *Transplant Cell Ther* . Jun 2023;29(6):356 e1-356 e7. doi:10.1016/j.jtct.2023.03.022

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