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Parental Decision-Making Regarding Consent to Randomization on Children's Oncology Group AALL0932

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Abstract

Background: Within pediatric oncology, parental decision-making regarding participation in clinical trials that aim to reduce therapy to mitigate side effects is not well studied. The recently completed Children's Oncology Group trial for standard risk acute lymphoblastic leukemia (AALL0932) included a reduction in maintenance therapy and required consent for randomization immediately prior to starting maintenance. At our institution, 40% of children enrolled on AALL0932 were withdrawn from protocol therapy prior to randomization due to parental choice. This study sought to identify factors that impacted parental decision-making regarding randomization on AALL0932.

Procedure: Parents of children enrolled on AALL0932 at our institution were eligible if their child met criteria for the average risk randomization. Parents were invited to participate in a 30–50 minute phone interview. Questions focused on factors that shaped parental decision-making about randomization, as well as their perspectives about the clinical trial experience more generally.

Results: Fear of receiving less therapy and subsequent relapse was the predominant reason to decline randomization. Reasons given for consenting to randomization included trust in the physician, altruism, hope for less therapy, and potential for fewer side effects. Parents also reflected on ways to support future families making decisions about clinical trial participation.

Conclusion: While many parents recognize the importance of clinical trials aiming to mitigate side effects, the fear of their own child relapsing with less than standard therapy may dissuade them from study participation. Recognizing and addressing these concerns will be important for enrollment and retention in future clinical trials.

Keywords

Decision-making; AALL0932; clinical trials; pediatric; oncology

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Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Introduction

The long-term survival of children with standard risk acute lymphoblastic leukemia (ALL) has drastically improved over the past 30 years, largely due to alterations in existing chemotherapy regimens.[1–6] These treatment modifications have been accompanied by increased risk for both acute and late side effects and increased burden for patients and families.[7–14] In the era of excellent outcomes for many pediatric cancers, along with the advent of targeted therapies, it is paramount to investigate therapeutic options that reduce adverse effects while maintaining outcomes.[14–17]

The most recently completed Children's Oncology Group (COG) clinical trial for standard risk ALL (AALL0932) used a 2×2 study design for average risk patients.[18] In one of the experimental arms, subjects were randomized to receive intravenous vincristine and oral dexamethasone pulses every 12 weeks rather than the standard 4 week interval during maintenance. The other study randomization compared standard to a higher starting dose of oral methotrexate.[18] A staged informed consent approach asked parents to sign consent forms three separate times. Consent for randomization occurred just prior to maintenance, approximately 8 months after initial enrollment. While study accrual goals were met and the trial was completed with adequate statistical power, 22% of children enrolled nationally (personal communication) and 40% of children enrolled at our institution withdrew from protocol therapy prior to randomization due to parental choice. This national refusal rate is similar to that seen on other COG ALL frontline trials with post induction randomization/ treatment assignments.[19–20] Potential adverse impacts of study withdrawal are selection bias, wasted resources and time, and longer time to trial completion.[21–23]

It is unclear why parents chose to withdraw after initial enrollment on AALL0932. The literature regarding decision-making for pediatric oncology clinical trials in general suggests that despite phase of study, the most common reasons parents give for agreeing to study participation are to help others, to help their child get the best therapy, and confidence in the recommendations and knowledge of the medical team.[23–26] Reasons identified for declining participation in pediatric cancer clinical trials include: too much to think about at time of accrual, concern regarding side effects, concern about treatment failure, difficulty understanding design, rationale and longer-term implications of the trial and medical mistrust.[23–28] Despite important information gleaned from past studies, limited literature explores parental perspectives and decision-making regarding clinical trials that investigate reductions in therapy. The present study was undertaken to investigate the perspectives and decision-making of parents whose children enrolled on AALL0932 at our institution. We hypothesized that the inclusion of a treatment reduction arm played an important role in their decision regarding randomization. The goal of this study was to gain insight that may optimize the process for clinical trial recruitment, enrollment, and retention, with focus on trials investigating a reduction in therapy.

Methods

Study setting/population/recruitment

Parents of children enrolled on AALL0932 at the authors' institution were identified through our clinical research database. All parents were invited to participate if their child remained eligible for the average risk randomization and spoke English.[18] Non-English-speaking parents were excluded due to limited access and resources for a research-trained non-English-speaking interviewer. Demographic information was gathered from the electronic medical record. Parents were recruited via a mailed letter and subsequent follow-up phone calls. This project was approved by the Oregon Health & Science University Institutional Review Board.

Data collection

Parents who agreed to participate took part in a semi-structured interview. The interview guide included both structured and open-ended questions, developed based on current literature and consultation with parents of children with cancer and other key stakeholders.[23–32] Questions were designed to elicit the factors that contributed to parental decision-making around consent to randomization on AALL0932, as well as parental perspectives about the clinical trial experience and clinical trials in general within pediatric oncology.

All interviews were conducted by phone by the same member of the research team (KP). Interviews lasted 30–50 minutes. Written informed consent was not required but parents received an IRB-approved information sheet; verbal consent was obtained over the phone. Participation was voluntary. Parents were provided a $25 debit card as compensation for their time.

Analysis

All interviews were audio-recorded and transcribed verbatim. In order to maintain anonymity, each participant was assigned a unique identification number. This information was stored in a password protected electronic file on a secure server and only one member of the research team (KP) had access to the list of names and unique identifiers. After all interviews were complete, transcripts were coded in NVivo using thematic analysis methodology.[33] In accordance with standard qualitative research methods, two members of the research team reviewed a subset of transcripts to develop a unified coding scheme and after reaching a high level of inter-coder agreement, coding proceeded independently.[34] The study team met to discuss study findings and discrepancies were resolved through consensus. Descriptive statistics were used to analyze responses for structured questions.

Results

At our institution 32 children were eligible for the AALL0932 average risk randomization. Two of these families were ineligible for our study because parents were Spanish-speaking only. Of the 30 families eligible for our study, 19 (63%) had at least one parent complete the interview. Four declined participation and seven could not be contacted. All participants, 20 parents of 19 children, were included in the analysis (Table 1). Thematic saturation was

achieved but did not drive sample size given that all willing and eligible parents were interviewed. Participants were predominantly mothers (85%) of white children (79%). Eleven parents had consented to randomization and nine had declined. Among those who were randomized, five children received standard frequency vincristine and oral dexamethasone pulses and six children received decreased frequency. Characteristics of children and parents who consented to randomization were similar to those who declined, with the exception of parental education. Seven of 11 parents who consented to randomization were less than college graduates compared with two of nine parents who did not (Table 1). All parents were interviewed between five to eight years after enrolling on AALL0932, at which time all children had completed therapy and were in first remission.

The key themes emerging from the semi-structured interview questions, described below, were organized into overarching categories that map onto different aspects and stages of parental decision-making, including: 1) Making the decision about randomization, 2) Providing informed consent, and 3) Ways to support future families. Responses to select structured interview questions are presented in Table 2, with representative quotes for identified themes presented in Tables 3 and 4. Quotes are labeled by group: randomized to standard therapy (RS) randomized to reduced therapy (RR), and not randomized (NR). Additional sample interview questions are included in supplemental material.

Making the decision about randomization

Most parents reported consulting additional people and resources before making their decision regarding consent to randomization, including nurses (10/20), other non-oncology physicians (4/20), friends (5/20), extended family (11/20), parents of other children with cancer (10/20), the internet (8/20) and one mother included the patient in the decision. Two parents did not discuss the decision with anybody. All but one parent felt their ultimate decision was made by either themselves alone or in conjunction with their significant other and/or physician.

Although some parents felt the decision was a “no brainer”, most said that the decision to consent to randomization on AALL0932 was difficult. One parent described it as “the hardest decision” of their life. Most (8/9) parents who declined and about half (5/11) the parents who consented endorsed still pondering their decision (Table 2). One parent reported still thinking about this decision almost every day. When asked to rank their level of anxiety, parents who did and did not consent to randomization reported similar levels of anxiety in making the decision. Those who did not consent reported a slightly higher level of difficulty in making the decision (Table 2). Several themes emerged with respect to the factors that contributed to the difficulty and anxiety associated with decision-making about randomization (Table 3).

Information overload and timing.—While some parents felt that not enough information was provided about the trial, others felt overwhelmed and overloaded with information. Some explained that making a decision about clinical trial participation in general in the midst of dealing with their child’s diagnosis felt like too much all at once. One parent said “It was a lot of information. It was absolutely overwhelming. I felt unqualified to

make the decision. I also felt that I was rushed into making decisions." (RR) Several parents commented that if the decision about randomization was at diagnosis, they would have declined.

The unknown of deviating from standard of care.—Many parents felt that agreeing to randomization on a clinical trial in general caused too much unknown. Multiple parents commented that they just wanted to stay on the proven course of therapy and described the challenge of making a choice that could deviate from the standard of care, especially when the outcome of that choice was unknown. One parent said, "I couldn't handle having my kid not get the standard of care which had been proven was working." (NR) For many, the challenge of grappling with unknown outcomes persisted even after the decision was made. Among those who chose not to consent to randomization, a couple of parents expressed guilt, wondering if their child might have had fewer long-term side effects if they had participated. One parent who consented to randomization often worried they had made the wrong choice because they still didn't know the study results.

Fear of less therapy and subsequent relapse.—Most (8/9) parents who did not consent to randomization stated this concern as their primary reason. Many parents worried that giving less chemotherapy could ultimately lead to a relapse. Others anticipated the decisional regret they would feel if their child participated and had a bad outcome. They could not fathom the guilt. One parent said, "I would never be able to live with myself knowing I made a choice that potentially caused relapse" (NR) and another commented, "If something happened where the cancer returned and he got less medicine than was normal, that would have been very difficult for me to live with as a parent." (NR) Although most parents were worried about less chemotherapy, one parent also worried about the possibility of more chemotherapy and did not want to risk any deviation from standard of care.

Hope for less therapy.—A few parents said that the chance that their child may receive less therapy and potentially experience fewer side effects was part of what motivated their consent to randomization. One of these parents expressed no concern about the experimental methotrexate arm because they understood that the dose would be adjusted based on patient's blood counts. One parent said, "the possibility for her to get equal care with less medication was really appealing to me." (RR)

Altruism.—All 11 parents who consented to randomization emphasized some perceived benefit (to future children, to science, their own child, giving back) as a key factor in their decision. Parents who consented to randomization mentioned wanting to help other children and families in the future, and some reflected that contributions of past families made them more inclined to do the same. Most parents acknowledged the importance of past clinical trials in informing current therapy. Some said that thinking of the families and children who took part before them made participation feel like the right thing to do. One parent said, "I felt like I was already reaping benefits from others, and so I needed to continue that." (RS*)* Multiple parents described guilt and a tension between what was right for their own child and their desire to help. One parent recalled the "pull between what I felt was the right decision for me and my child versus what I thought we should do." (NR)

Trust in their physician.—Most parents who consented to randomization commented that a significant contributing factor was the trust they had in their pediatric oncologist. Some said that although they felt that the final decision was their own, their physician provided them the necessary information. One parent described making the decision to consent for randomization "because her [child's] doctors felt like this was a good decision and we trusted the doctor…I did feel very confident all along that the doctor would not do anything that was going to be dangerous." (RS)

Providing informed consent

Overall, parents were satisfied with the consent process (Table 2). Although all parents remembered at least parts of the informed consent process, only two parents recalled the three staged consents. When reminded about the latter, parents did not feel their choice about consent to randomization was influenced by the interval between consents and many mentioned appreciating this approach. Some said that the staged consent process was helpful and enabled more time to talk to the provider, seek information on their own, and reflect. One parent said, "I appreciated that we didn't have to make the decision [regarding randomization] on the day of diagnosis because that's a pretty emotional time. I needed the extra time to think about it and read everything." (NR)

Ways to support future families

The majority of parents (16/20) said they would recommend that other parents consider participation in a clinical trial. The other four parents expressed a desire not to interfere with another parent's decision-making. Overall, most parents felt that their clinical trial experience, whether or not they consented to randomization, went well. All parents were asked to identify areas for improvement or additional support for families as they make decisions about clinical trial participation in the future. Parents offered the following types of recommendations (Table 4).

Enhancing communication with physician.—A few parents didn't feel extra resources were needed and that an open discussion with a physician and confirmation of comprehension was sufficient. Others suggested ways to improve or enhance the way information is presented and communicated, including: having the same physician discuss the trial with family at every step, separate visits to discuss the clinical trial when the child wasn't present, and taking more time to explain the study. Some parents suggested providing more education about the basics of clinical trials, establishing a standard process to provide trial updates and results and the importance of explaining what the next step would be if their child recurred during or after the trial.

More information on long-term risks/benefits.—Although many parents had a hard time with the decision to consent for randomization on this trial, most parents felt that clinical trials aiming to mitigate long term side effects are important (Table 2). However, many said it could be difficult for parents to agree to potentially less treatment, especially when the cure rate with the standard care is already high, as is the case for standard risk ALL. Parents suggested one way to lessen this challenge would be to fully inform parents about long-term side effects of the standard treatment and to help them understand that

participating in a trial could potentially decrease those effects. Others mentioned that providing more data about why the study is being done and potential benefits of participating in the trial would be helpful.

Other parents as a resource.—Multiple parents supported contact with other parents. They felt hearing from another parent who had been through the same decision may provide needed support. Other parents suggested it might be helpful to have written or video testimonials from parents who have made the decision before.

Easy to understand written, web or video materials.—Some parents supported a short study handout written in layman terms that they could take home and share with family members not at the visit. Others liked the idea of a video or website that explained clinical trials in general and then specifically explained the clinical trial their child was being offered.

Discussion

Improved cure rates for childhood cancer often come at the expense of long-term health and quality of life, therefore clinical trials need to address these long-term effects while optimizing outcomes.[14–17] For future studies to succeed parents must agree to enroll and complete the study protocol. Our study is unique in that it specifically focuses on parental decision-making about reduction of therapy while maintaining excellent outcome rather than escalation of therapy to improve outcome. For the cohort of parents in our study, worry about relapse and the subsequent associated guilt was a primary factor in their decision-making. There were also several parents excited by the prospect of less chemotherapy and fewer side effects. The methotrexate randomization that compared standard to a higher starting dose was not a prominent theme in their decision-making. Consistent with published studies, parents who consented to randomization had lower education levels than those who did not.[27] As in other studies, we found that altruism and trust in their physician also contributed to parental decision-making.[23–24] Our study describes many of the reasons for parents' decisions, as well as parents' perspectives on ways to support future families for clinical trial decision-making.

Published research regarding informed consent in pediatric oncology have focused on the quality of informed consent and parental understanding of clinical trials. Parents generally lack accurate understanding of the intricacies of the consent process or specifics of study participation.[29,31–32] Although there is limited literature looking at the staged consent approach in pediatric oncology, Angiolillo suggested that using a staged consent approach can help investigators obtain a more truly informed consent.[35] Given the interval between participation on AALL0932 and the current study, we were not able to assess parental understanding or the impact of the staged consent; however, we did find that most parents felt satisfied with the consent process and that the staged consent allowed them more time to ask questions, to feel like they understood the study and to make their decision.

Prior studies have found that high quality, individually-tailored information, open communication and psychosocial support, and adequate time to make the decision can help

support clinical trial decision-making.[36–37] Our study supports past findings and adds specific suggestions including: access to understandable written materials, web and video-based materials, access to other families willing to talk about their clinical trial experiences, and suggestions for improving communication with physicians. In the time that has elapsed since parents were asked to make this decision, multiple resources to help support families have emerged or are in development. These resources include websites with family narratives about experiences with childhood cancer and clinical trials, websites with information about and logistics of clinical trials, and studies investigating the use of decision aids for clinical trial decision making.[36,38–43] Concise lay language summaries for pediatric oncology clinical trials are not consistently available and, given the results presented, should be considered in the future.

There are several merits to our study. Using qualitative methods and a mix of structured and open-ended questions allowed us to capture more data than by simple survey-based methods. We were able to capture in-depth information from the dynamic dialogue that occurred during interviews. The relatively high response rate (63% of eligible participants) and the fairly equal distribution between participants who chose and declined to consent for randomization are other strengths. We interviewed all willing participants which ultimately provided enough data to reach thematic saturation in our qualitative interviews.

There were also limitations to our study. Although we captured a broad range of perspectives, our study is from a single institution, limiting generalizability. The narrow age range (1–9 years old) of children eligible for AALL0932 may also hinder generalizability of results to older children, adolescents and young adults. Selection bias may have influenced our findings as parents with strong opinions may have been more inclined to participate. Given that parents were interviewed about an event that occurred five to eight years ago, there was likely recall bias, although perhaps improved reflection as well. Given the study eligibility, concerns from parents who declined the upfront enrollment on AALL0932 were not captured. We excluded the two Spanish-speaking families and, thus, were not able to get perspectives from an important population within pediatric oncology that has been shown to have lower clinical trial enrollment rates.[44–46]

In order to make continued therapeutic advances in pediatric oncology, clinical trial participation is essential. For studies to have meaningful results in desired timeframes, optimal enrollment and retention is critical. The future of pediatric oncology clinical trials includes both efforts to minimize exposure to toxic therapies through reductions of therapy as well as the introduction of novel therapeutic strategies with the potential for less toxicity and better outcomes. Many of these studies will contain randomizations. Recognizing that parental concerns significantly impact decision-making and incorporating suggestions to address these concerns may improve the consent process and, thereby, be beneficial to study enrollment and retention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Abbreviations Full Term

ALL	Acute lymphoblastic leukemia
COG	Children's Oncology Group
RS	Randomized to standard therapy
RR	Randomized to reduced therapy
NR	Not randomized

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Table 1

Characteristics of participating parents and children

Child (N=19)	All (N=19)	Randomized (N=11)	Declined (N=8)
Age at diagnosis, y, n			
1–3	11/19	6/11	5/8
4–6	6/19	5/11	1/8
7–9	2/19	0/11	2/8
Sex, n			
Female	13/19	8/11	5/8
Male	6/19	3/11	3/8
Race			
White	15/19	8/11	7/8
Non-White	4/19	3/11	1/8
Ethnicity			
Non-Hispanic	18/19	10/11	8/8
Hispanic	1/19	1/11	0/8
Parents (N=20)	All (N=20)	Randomized (N=11)	Declined (N=9)
Relationship to child			
Mother	17/20	9/11	8/9
Father	3/20	2/11	1/9
Age at child's diagnosis, y, n			
20–24	1/20	1/11	0/9
25–29	5/20	3/11	2/9
30–34	8/20	5/11	3/9
35–39	5/20	2/11	3/9
40–44	1/20	0/11	1/9
Education			
Less than college graduate	9/20	7/11	2/9
College graduate	6/20	2/11	4/9
Graduate or professional school	5/20	2/11	3/9
Marital status during treatment			
Married	15/20	8/11	7/9
In a relationship	2/20	2/11	0/9
Divorced	3/20	1/11	2/9
English 1st language			
Yes	18/20	10/11	8/9
No	2/20	1/11	1/9

Table 2

Parental answers to structured interview questions

Questions		All (N=20)	Randomized (N=11)	Declined (N=9)
How satisfied were you with the consent process? (parent asked to rank on a scale of 1–10, with 10 equaling extremely satisfied)	median (min, max)	8.5 (6,10)	8 (6,10)	9.5 (8,10)
Do you think about the decision of whether or not to randomize now? (yes or no)	Answered yes	13/20	5/11	8/9
What was your level of anxiety associated with the decision of whether or not to randomize? (parent asked to rank on scale of 1–10, with 10 equaling extreme anxiety)	median (min, max)	6.5 (1,10)	7, (1,10)	6, (1,10)
How difficult was it to make the decision of whether or not to randomize? (parent asked to rank on a scale of 1–10, with 10 equaling extremely hard)	median (min, max)	7 (1,10)	5 (1,10)	8 (4,10)
Rate the importance of clinical trials aiming to decrease long term side effects (parent asked to rank on a scale of 1–5, with 5 being extremely important)	median (min, max)	5 (3,5)	5 (3,5)	5 (3,5)
Rate the importance of clinical trials aiming to decrease short term side effects (parent asked to rank on a scale of 1–5, with 5 being extremely important)	median (min, max)	4 (2,5)	4 (2,5)	4.5 (2,5)

Table 3

Making the decision about randomization

Theme	Examples
Information overload and timing	• "It's a shocking volume of information that you're trying to take in and then make a decision about a clinical trial and determine what is best for your child. I don't know, you know... It's hard. It's hard." (RS) • "It's such a hard time to make any decisions at all...I remember at the time telling my husband that it was hard for me to like, pick out what clothes to wear because I was so overwhelmed...with your child's illness and all the decisions that you're being asked to make and all of the different possible outcomes. So I think just any decision is really challenging." (RS) • "The unfortunate confines of the timing and the kind of hysterical state of mind of the parents at the time and the fact that it's asking you to sign up for something like that...it's hard from the parent's point of view in a time crunch to decide to do something." (RR) • "Yeah, I think it would have been, if I had to decide like that first day, I don't know if I would have done it because it's like complete overwhelm." (RR)
The unknown of deviating from standard of care	• "She was first diagnosed and we were told that the survival rate was like 90 percent and that felt really positive and secure. And then the idea that we were going to not necessarily go the established course made me just wonder if we were going to do the wrong thing." (RS) • "We were grappling with it so much and that the sort of gut reaction of like I can't allow my kid to be given less of the drug...so in the end like to truly have her be a guinea pig, to have an experiment done on her was something I couldn't do." (NR) • "There were just too many variables. I guess there was too many unknowns...I just feel like one more thing that we didn't have control of when we were like kind of grasping at straws already." (NR) • "Yeah, there was a proven track that showed this does work, so we wanted to see a proven track record of this does work... we think maybe we could do better with this therapy but we didn't know. We didn't want to take that chance, we wanted to stay on the proven track record of we know this works." (NR)
Fear of less therapy and subsequent relapse	• "And then also just in a society where more medication means more healthy. That's also a difficult part of choosing something that has less just because of the mindset that you enter into the experience with." (RR) • "I felt like if she was on the lowest one and she relapsed, I would've felt guilty. So, that's the only reason. That possibility was really stressful for me." (NR) • "If we had a guarantee she would get the same amount of chemo or more, we probably would have stayed on it. But the question was if she got the less option, that was not what we wanted to... So, selfishly or not, I couldn't handle my kid not doing all those treatments." (NR) • "I think the primary goal for parents is they don't want the cancer to come back. So, anything that increases that chance is scary. When you know the current treatment is probably successful as it was. You know, you don't want to – you know, that's a hopeful number. So, to do something to mess with that is like scary. You know, for me, I was just thinking of I want to make sure the cancer is gone, and gone for good. But then, I think afterwards, taking into account for the rest of her life, as well, she's going to have the effects of all the chemo that she's had." (NR) • "So, we decided not to join the study at all, because we wanted to make sure our son got at least the same standard or more medicine." (NR)
Hope for less therapy	• "Because if she got less medication then maybe she would suffer less." (RS) • "Just knowing that if we did do the study, there was a chance of him doing less chemo anyway, which was always kind of a nice thought." (RR) • "A less toxic option was very appealing…we had an opportunity to make the treatment less toxic and less harmful." (NR)
Altruism	• "The thing that stuck out to me, I think, mostly was that if they did not do these studies and if people did not participate, then they wouldn't be able to fine-tune the medication and the treatment." (RS) • "I didn't feel like I fully understood what I was getting into completely, but I felt that it was still the right thing to do." (RS) • "Another reason was to help benefit the kids who came before him who were going through the same thing as him. Hopefully, things would come out well so he would not have to receive as much chemo and have that be the new norm." (RR) • "Just for the research purposes for her future kids...advancements in cancer treatment for children." (NR) • "We were very concerned about science. Like we definitely have this feeling of like I'm not going to take all of this research that was done that is benefitting my kid and then close the door behind us." (NR)
Trust in their physician	• "The doctor offered and we decided to, because they explained how important it was for the treatment, for the trial, how important it was because the kids were able to be treated better and have better options for the treatment. The doctor explained and we decided." (RS) • "Well, first of all we trusted our doctor and his decision.... that was the main thing." (RR) • "There's no reason why we couldn't participate. The risk was calculated and our doctor felt comfortable with putting any of her patients into it." (RR)

RS=Randomized to standard chemotherapy regimen

RR=Randomized to reduced chemotherapy regimen

NR=Not randomized

Table 4

Ways to support future families

Theme	Example
Enhancing communication with physician	• "So to have doctors that care and care enough to know how to talk to you so that you can hear, you can comprehend and you can be part of the conversation is so important." (RR) • "For me, the discussion with the doctor was sufficient." (RR) • "Also, to really let the parents know that they can quit at any time I think is important. My experience while talking to other parents is that they really felt like that once they were on board they couldn't really quit." (RR) • "I think it's a clear communication about what the study is up front and especially concise. I think those are the biggest." (NR)
More information on long-term risks/ benefits	• "There is so much that is already unknown it is just adding more unknown but if you can give them all of the side effects of the known it would definitely aspire to do the unknown. I mean if you explain the motivation is to decrease the long-term impact that is a win." (RS) • "More advice on the study alternatives, the study options and that the data exists. Obviously it's not going to be as high a confidence as the standard of care, but if what somebody had said was 80 percent or 90 percent confidence we think this is the better cure rate with no compromise in cure rate and less toxicity, I would have said absolutely. If somebody had some numbers, if somebody had sort of the basis of the study had more data behind it, I think that would be what would have changed my mind." (NR)
Other parents as a resource	• "It would have been helpful to have other families that have gone through a clinical trial to talk to." (RR) • "Testimonials from other parents that have gone through it is something that is very helpful as a parent new to the situation." (NR)
Easy to understand written, web or video materials	• "You know, a brochure, an infographic or a little video that has like, the four strands or four arms and like, your child can be X, Y, B, or C that I could have had my friends and family review." (RS) • "A smaller booklet of information to look at. Just a more understandable version. It's difficult to understand the huge packet even with some medical knowledge." (RR) • "It would be great to walk away with something in your hand that describes it because a lot of the language that's used and the references make sense during the conversation but are lost as soon as you walk away." (RR) • "You could just get a website. I think that a website would be a huge thing for people to be able to link to and understand." (RR) • "All the information possible in a format that we can understand is really huge when it comes to just your kids and making the best choice... something like a laymen's terms packet would be good." (NR) • "If there was like a YouTube video that's supposed to explain what research studies are, the different types, what type this one is, and what it means to participate." (NR)

RS=Randomized to standard chemotherapy regimen

RR=Randomized to reduced chemotherapy regimen

NR=Not randomized