Published in final edited form as:

J Empir Res Hum Res Ethics. 2012 April ; 7(2): 51–59. doi:10.1525/jer.2012.7.2.51.

Negotiating Decisions during Informed Consent for Pediatric Phase I Oncology Trials

Patricia A. Marshall,
Case Western Reserve University

Ruth V. Magtanong,
Cleveland Clinic

Angela C. Leek,
Cleveland Clinic

Sabahat Hizlan,
Cleveland Clinic

Amy D. Yamokoski, and
Cleveland Clinic

Eric D. Kodish
Cleveland Clinic

Abstract

During informed consent conferences (ICCs) for Phase I trials, oncologists must present complex information while addressing concerns. Research on communication that evolves during ICCs remains largely unexplored. We examined communication during ICCs for pediatric Phase I cancer trials using a stratified random sample from six pediatric cancer centers. A grounded theory approach identified key communication steps and factors influencing the negotiation of decisions for trial participation. Analysis suggests that during ICCs, families, patients, and clinicians exercise choice and control by negotiating micro-decisions in two broad domains: drug logic and logistics, and administration/scheduling. Micro-decisions unfold in a four-step communication process: (1) introduction of an issue; (2) response; (3) negotiation of the issue; and (4) resolution and decision. Negotiation over smaller micro-decisions is prominent in ICCs and merits further study.

Keywords

informed consent; informed consent conversations; pediatric oncology Phase I trials; decision-making

Oncologists who are discussing a Phase I cancer trial face a formidable communication challenge. They need to present information about the trial in a manner that is easily understood, while also addressing concerns raised by patients and family members. In Phase I studies, patients have a very poor prognosis with no curative treatment options. The informed consent process may be influenced by psychological distress experienced by patients and families, increasing their vulnerability and creating challenges to

comprehension and decision-making. Physicians conducting Phase I oncology clinical trials have little guidance in managing the informed consent conversation in this context. However, in their review of 12 studies on communication during informed consent for Phase I clinical trials, Jenkins et al. (2011) found that this topic was consistently reported as difficult for clinicians to discuss. Moreover, previous research indicates that patients and families may be unwilling to discuss issues such as end-of-life care because of their hope for a cure, desire to extend life, or because of misunderstandings associated with therapeutic misconceptions (Kodish, 2003; Hinds, Pritchard, & Harper, 2004; Miller & Joffe, 2008; Sulmasy et al., 2010). Additionally, there may be discrepancies between what is actually said by clinicians and what is heard and interpreted by patients and their families (Kass et al., 2008; Jenkins, Anderson, & Fallowfield, 2010). Although research on informed consent for pediatric clinical trials has expanded (Kodish et al., 1998; Simon et al., 2003; Yap et al., 2010), the actual communication process that takes place during the informed consent conference (ICC) remains unexplored. Most studies assessing communication and comprehension are limited to retrospective interviews and survey instruments (Agrawal et al., 2006; Cohen et al., 2007; Finlay & Casarett, 2009). However, limited data from analyses of actual Phase I trial discussions suggest that key components of the communication process are not captured by these methods (Kass et al., 2008; Jenkins et al., 2010). While audiotaping as an alternative method has been used to improve communication in clinical settings before (e.g., Koh et al., 2007), its use for assessing the communication process itself has not been common.

Pediatric oncologists presenting Phase I clinical trials to their patients and families encounter multiple ethical challenges that are inherent to the design of Phase I studies. Research policies consider young children to be vulnerable research subjects because they cannot make a truly autonomous decision, and are dependent upon another person, most often their parents or legal guardian, to protect them from research risk (Coleman, 2009). With Phase I studies, clinical benefit for the patient is highly unlikely because the primary goal is to determine a safe dose for future research. Difficulties arise in communicating the research goals and low prospect of direct benefit, to parents and older children, and this can lead to a therapeutic misconception (Kodish, 2003; Miller & Joffe, 2008; Sulmasy et al., 2010). This therapeutic misconception that the trial will benefit their child, when it is unlikely, raises challenges to fully informed consent.

Another ethical concern as defined by the Belmont Report (Department of Health, Education, & Welfare, 1979) is the integration of research and clinical care, and how the goals of each demand different considerations. This is apparent in pediatric oncology, where the physician is often both clinician and researcher (de Vries et al., 2011). As a clinician she is obligated to promote the best interests of her patient, while as a researcher she is dedicated to developing evidence that will contribute to the health of future patients. The ethical dilemma centers on (1) the role-tension between researcher and clinician, (2) how these roles can impact communication and relationships with the patient and family, and (3) the physician's own struggle to do the right thing.

Patients and Methods

Coordinated by the Cleveland Clinic Department of Bioethics, this research project is a multi-site study of informed consent at six pediatric oncology programs in the United States conducting Phase I trials. The overall goals are: (1) to understand the communication process between parents and clinicians; (2) to assess comprehension of parents and older children after ICCs; and (3) to examine perspectives of clinician-investigators about the informed consent process. The ICCs involved clinicians (physicians, nurses, and other healthcare team members present during the ICCs), parents and other family members, and

in most cases, children with diagnosed refractory cancers. The study utilized a mixed methods design that generated quantitative and qualitative data for analyses. ICCs were directly observed and audiotaped by trained research assistants. The audio-recordings of the ICCs were transcribed verbatim and transcripts were imported into Atlas.ti, a software program for qualitative analysis. Demographic information was obtained via parent interview after the ICC.

Institutional review board approval was obtained from each site. Families were eligible for the study if they were considering entering their child onto an open pediatric Phase 1 oncology clinical trial. Patients who were English and/or Spanish speaking, aged from birth to age 21, and diagnosed with refractory or relapsed cancer were considered for inclusion. The process of obtaining informed consent from physicians, families, and patients was carried out with high ethical regard for the sensitive nature that surrounds Phase 1 trial discussions. Written consent was first obtained from the physicians and medical staff who were willing to take part in this research. This then implied their consent to participation in the direct observation of the research project. In order to approach families for this research, a member of the healthcare team would notify the site research assistant of a family's interest. The research assistant would then make contact with the family to obtain their written informed consent for this study. The patients' written consent was obtained if they were over the age of 18 in tandem with their parents, and verbal assent was solicited from patients over the age of 7. It was made clear that all parties who agreed to participation in this research study could decline their further involvement at any time.

In this paper, we report on data analyzed for 16 ICCs obtained from a stratified random sample of 49 ICCs. The stratified random sampling was based on the following criteria: (1) institutional referral pattern; (2) past clinical trial experience; (3) whether a *patient* interview was conducted after the ICC; and (4) clinical trial/data collection site. These criteria were chosen to ensure that the 16 ICCs reflected a representative sample of the larger set of ICCs.

Transcripts from the 16 audiotaped ICCs were analyzed using a grounded theory approach (Corbin & Strauss, 2008). Primary coding involved a line-by-line conceptual labeling of each transcript in its entirety. Conceptual labels were then compared to each other to refine codes and eliminate redundancy. Primary coding revealed factors influencing the negotiation and communication processes involved in parents' and patients' decision-making during ICCs. Seven coding domains were applied: quality of life, therapeutic misconception, side effects, past clinical trial experience, cancer experience, healthcare relationships, and family issues. A secondary coding was initiated to assess conditions, responses, and outcomes of the communication process within and among these coding domains. From this secondary coding, a conceptual framework was developed focusing on the communication process among clinicians, parents, family members, and older patients participating in the ICCs. This conceptual framework was used as a guide to further refine concepts and validate the steps in the communication process in a third coding pass that looked at specific segments of each transcript.

Table 1 summarizes characteristics of patients and parents participating in the 16 ICCs. Sixty-nine percent of the patients were male. Forty-four percent of the parents were college graduates. Eighty-one percent of parents reported that their child had previously participated in a research study for his/her cancer, but only 25% reported having participated in a Phase I study.

Results

The ultimate decision in the ICC is whether or not to participate in the Phase I trial being offered. All 16 ICCs concluded with an affirmative decision for trial participation. However, our findings suggest that during the ICC there are a series of smaller decisions, referred to here as “micro-decisions,” that are negotiated, allowing parents, family members, and older patients some control in determining particular aspects of their trial participation.

Analyses of ICC data suggest two broad domains of micro-decisions where parents and, if possible, their children with cancer can exercise choice in the decision-making process (Table 2). The first micro-decision domain concerns drug logic and logistics in the Phase I trial. This domain of decision-making is represented by four categories: (1) issues associated with drug efficacy and reasons the trial was offered to the patient; (2) issues associated with drug delivery, including methods and timing; (3) monitoring toxicity for side effects, quality of life, and prevention of infections; and (4) location of drug availability, whether provided at the hospital, an outpatient clinic, or at home.

The second micro-decision domain focuses on scheduling drug administration and is represented by two categories: (1) dates and times of administration and (2) effect on daily activities. The distance to travel for drug administration, family responsibilities, and social obligations influence micro-decisions regarding scheduling dates and times for participation in the Phase I trial. Data analysis suggests that issues associated with daily living such as a child’s school and sports activities, a parent’s work schedule, and family relationships also influence the negotiation of micro-decisions around scheduling.

We discovered that micro-decisions associated with choices relevant to drug logic and logistics and scheduling drug administration are negotiated in a four-step communication process influenced by a range of factors concerning family life, social activities, quality of life, management of side effects, and the patient’s experience with cancer and clinical care (Figure 1). First, an issue is presented as a statement or question by the physician, parent or family member or, in some cases, the patient who is an older child. Statements or questions generally focus on reasons for participating, various components of a Phase I clinical trial, and the impact of trial participation. Second, other participants in the ICC discussion respond to the statements or questions. Four categories of responses were identified from our analyses: (1) affirmation (agreement); (2) uncertainty (the speaker hesitates or seeks reassurance); (3) deflection (the speaker redirects or changes the topic); or (4) rejection (disagreement). Third, the issue is negotiated and discussed. During the negotiation process, participants draw on factual information relevant to the Phase I trial, family and social issues, a patient’s physical condition, prior response to therapy, and emotional and psychological experience related to the cancer journey. In the fourth step, a micro-decision is explicitly vocalized or implicitly resolved at the end of the ICC when patients and families formally agree to participate.

Case Examples

The following transcripts from two ICCs illustrate the interactive process of communication that underlies the negotiation of micro-decisions. The first case describes the negotiation process for micro-decisions representing the domain of Drug Logic and Logistics. The second case example describes the negotiation process representing the micro-decision domain of Scheduling Drug Administration. These examples highlight the range of issues drawn upon to provide information that informs the discussion or that influences ICC participants in making a decision during the negotiation process.

Case 1. Micro-Decision Domain: Drug Logic and Logistics—

Issue: *Mom.* So, why are you doing the study?

Response: *Physician.* We don't have to. Um...

Negotiation: *Mom.* Yeah, but why would you do the study even?

Physician. For a chance, even though it is a low chance.

Dad. It is our only chance.

Physician. Well, it's the only ... um, study I have open right now and that doesn't mean I am just taking whatever is available. It happens to be a very reasonable study. It is a drug that has shown activity in [this tumor] in the laboratory...and the preliminary results look encouraging but you know, we don't have all...it has just recently been developed. It is an oral drug. It doesn't have a lot of side effects [...] so you know, we have to focus on quality of life here, that is clearly paramount. Um but...given how well this is generally tolerated and the fact that it is oral and we have, you know, it is more visits. There is no question that it is more visits. We would have to see you once a week but many times in a time like this, we want to see her once a week anyway because things are changing.

Response: *Mom.* Yeah, I noticed it is a whole year that this...say another study comes up, she would not be eligible for it?

Negotiation: *Physician.* No, she would. So, we would treat her on this for a month...And then we would re-evaluate with an MRI scan and if she is worse or the scan looks worse then we could consider other studies...But there is no study that is better or no drug that is better than any others. So in many ways some of the decision has to be based on quality of life. You know, what's gonna cause the most ...side effects. Now, whenever we are dealing with an experimental drug, we don't have a great handle on um, the side effects many times... [A]nd this was the same for the capecitabine. [We] treat three children at a certain dose and if they don't have bad side effects then the next three children get a higher dose, the next three children get a higher dose. So um, this study probably has been open for about a year. I think they are at the second or the third dose level...and so far they have not really seen any significant side effects.

Decision: *Mom.* OK.

Case 1 Analysis: The first issue is presented by the patient's mother, who asks why the physician is offering the study. The physician responds with uncertainty, immediately suggesting that the choice of participating in the Phase I trial is still open for discussion. The negotiation process begins with the mother affirming the physician's remark, but she persists with her question about why the study is being offered as an option. Her repeated question prompts both the physician and the father to make transparent in the discussion the underlying but profound motivating force of hope in decisions to join Phase I clinical trials. The physician's reply to the mother is straightforward, acknowledging that there is a "chance...even a low chance," and the father affirms this remark, but takes it to a deeper and starker reality when he says, "It's our only chance." The meaning of "chance" in this exchange is unspoken but appears to be understood by the participants. We can infer that the physician and the father may hope for a "chance" of a cure, or at the very least, an extended life, perhaps a better quality of life.

Following this interaction in the negotiation process, the physician provides another reason for participating, suggesting that it is the only trial option available at the moment. He then provides information about trial participation that is both persuasive ("It happens to be a

reasonable study...preliminary results look encouraging”) and factual (“It is an oral drug... [with few] side effects...[it requires] more visits”).

Case 2: Micro-Decision Domain: Scheduling Drug Administration—

Issue: *Physician.* What day could we start next week?

Response: *Patient.* I wouldn’t be able to go to California because I have to be here, right?

Negotiation: *Physician.* Your cancer, we’ve been doing this for a long time, right?

Mom. Well, she was only going to California for one week.

Response: *Patient.* But I have to be there for...

Negotiation: *Physician.* You need to stay...’Cause see, ...the thing is that this study, like all these Phase I studies, is mostly about studying the medicine. We really hope that you get some benefit out of it, but the real purpose of...these studies is to study the medicine and we need, if you have something go wrong we need...to have you nearby so we can figure out what went wrong and so we can report on side effects of the medicine. The more intensive monitoring is in this first month. That’s when we think if something really is going to go wrong, it’ll happen then.

Mom. Now one thing you did say is you’re testing to see how it clears out of the body. I mean how will you test that if she’s taking it every day?

Physician. [talks about blood draw schedule] And that’s how we sort of measure how your body clears the medicine out of your system.

Mom. [to daughter] So you need to think about that, right?

Physician. Is this a deal breaker?

Response: *Patient.* Well not really, I guess. Just that I already figured it out before I got here what I ...

Negotiation: *Mom.* So your decision, honey. What? I can’t make that for you.

Patient. [to mother] Can you help? [laughter]

Mom. I don’t know. Well you haven’t made [bought] your ticket yet. Couldn’t you just make it for after four weeks? ... Can I see a calendar? ... When would she start?

Physician. Well we would start it next week and we’d have to pick a day that works for you, but also a day that we could do this pharmacokinetics stuff.

Mom. So probably the 14th, the Wednesday, ’cause I can come ... You could go the....week of the 16th to California then.

Decision: *Patient.* Mom ... Okay, I’ll do it.

Case Analysis 2: In this case, the physician raises the issue of when to start the clinical trial. The patient responds with uncertainty when she brings up a possible conflicting engagement, a trip to California. In negotiating when to start, key factors are introduced such as the patient’s extensive treatment history and quality of life. The physician begins the negotiation by reminding the patient that “she’s been doing this for a long time.” In other words, cancer treatment is a priority and a commitment has been made.

Although the primary purpose of the clinical trial is to “study the medicine,” the physician brings the focus back to the patient by emphasizing patient safety through monitoring. Still uncertain, the patient turns to her Mom for guidance. Mom reminds her daughter that she has not bought the plane tickets, so the trip to California is flexible, and thus can be postponed to a later date, while the clinical trial starts now and requires a sign of commitment. Expressing resignation, the patient postpones her trip to California.

Discussion

Effective communication is the foundation of successful informed consent. Our study of communication during ICCs suggests that a process of negotiation over smaller, micro-decisions occurs. The decision to participate in the trial may be a *fait accompli* prior to the informed consent conversation for some families, but these micro-decisions may serve to reframe the discussion and provide some measure of control. An important finding of our study reveals that patients, family members, and clinicians negotiate micro-decisions over issues that are amenable to exercising choice without impacting Phase I trial goals. Micro-decisions were associated with treatment, the logistics of drug regimens and scheduling issues, and were heavily influenced by considerations such as quality of life and daily activities.

The ability to make choices regarding flexible aspects of participation in Phase I oncology trials can empower patients and families, enhancing their experience with the decision-making process, particularly when treatment options are severely limited and the life-death implications for patients are significant. Our analysis indicates that micro-decisions unfold in a four-step communication process beginning with the introduction of an issue by any participant in the ICC conversation, and followed by a response from other participants that expresses affirmation, uncertainty, deflection, or rejection of the issue presented. The issue is then negotiated in a discussion in which participants present information to reinforce their positions. Finally, a decision is reached regarding the specific issue. Understanding this communication framework may be a useful tool for clinicians as patients and families attempt to exert some control over their experience in Phase I oncology trials.

Our findings corroborate recent studies that suggest patients in Phase I oncology trials are neither inexperienced nor uninformed about their options. Rather, patients and families have extensively investigated and assessed the alternatives, and have discussed their cancer status and options with more than one physician (Agrawal et al., 2006; Cohen et al., 2007). The knowledge and experience that patients bring to Phase I consent discussions reinforces the collaborative nature of the doctor-patient relationship in the decision-making process regarding study participation. Through this collaboration, the negotiation of micro-decisions creates opportunities for patients and families to control particular aspects of the trial experience.

One potential limitation of this study is the small sample size. However, the sample is adequate to reach saturation given the narrow focus of analysis (Morse, 1991). The analytical approach used on transcriptions of the audio-recordings of ICCs ensured that the full range of thematic domains relevant to decision-making were addressed (Glaser & Strauss, 1967). Other limitations include the fact that some discussion of the trial may have taken place either before or after the audiotaped segment(s) we were able to capture, and the concern that ICCs taking place at these six sites may not be generalizable to other centers.

Best Practices

Our findings illustrate a range of anxieties, tensions, and concerns expressed by parents and their children during ICCs. The study reveals the negotiation of decisions through a

collaborative process of communication that unfolds as a final decision is made. The micro-decisions that are represented in the communication framework we developed may be a useful tool to help clinicians understand patients' and families' attempts to exert some control over their experience in pediatric Phase I oncology trials. Moreover, attention to the process of micro-decisions that are embedded in the ICCs is congruent with the emphasis on the patient-centered model of care that should be practiced in oncology clinical trials.

Navigating the micro-decisions that occur during ICCs and obtaining informed consent for Phase I trials is ethically challenging for pediatric oncologists. These difficulties include the design of Phase I trials, the vulnerability of the research population, and the intertwined roles of physician-investigators. In order to obtain valid and ethically sound informed consent, attention to the communication that evolves during ICCs needs to be assessed. Parental comprehension could be improved through clear explanations of the trial, with multiple reiterations, and open-ended questions. Allowing the physician to define the role of clinician as researcher, and vice versa, could also benefit the informed consent process.

Research Agenda

Because these are difficult and high-stakes discussions, it is important to carefully examine the communication process as it unfolds within ICCs for pediatric Phase I oncology trials. Future empirical research using qualitative *and* quantitative methods is needed to assess the diverse range of factors influencing the negotiation process and their relative importance in micro-decisions that occur during informed consent conversations in Phase I oncology trials. Research is also needed to identify the applicability of the negotiation of micro-decisions in ICCs for adult Phase I oncology trials. In addition, there is a need to develop and evaluate strategies that reinforce clinicians' effectiveness in addressing concerns raised by patients and families during the negotiation of decisions. One fruitful approach, building upon the work of Koh et al. (2007) in the neonatology context, might be to assess the value of providing a tape of the ICC to families after the consent process. Finally, moving beyond Phase I oncology trials, future research examining the negotiation of micro-decisions in ICCs for other types of clinical oncology trials may reveal important similarities and differences in the communication process that occurs.

Educational Implications

Findings from this study highlight the importance of educating physicians, nurses, and other team members for Phase I oncology trials about the negotiation of smaller decisions that take place during ICCs over topics such as drug regimens and scheduling. The development of educational strategies that focus on micro-decisions and the communication process that occurs in informed consent conversations would accomplish two important goals. First, training on negotiating micro-decisions during ICCs emphasizes the value patients and families may attach to exerting some control over decisions that would not impact the goals of a Phase I trial. Being sensitive to the importance of a patient's or family's need to exert control and make decisions in a situation where choices are diminished can prevent needless attempts by physicians and other team members to take a rigid position over an issue that is amenable to flexibility. Second, training on the communication process during the ICC augments the collaborative partnership that is key to the success of a model for patient-centered care.

Innovative and creative approaches to training should be developed. Actual ICCs, for example, could be audio-taped with the permission of patients and family members, and used as teaching tools to increase understanding of the language and affect of participants in the discussion (Yap et al., 2009). Particular attention should be given to the dynamic process of negotiation that unfolds as decisions are made. Greater understanding of the

communication process—including micro-decisions—has the potential to heighten sensitivity to the concerns of patients and family members as they confront the life-death implications of participating in Phase I oncology trials.

Acknowledgments

This research was supported by the National Institutes of Health (NIH) by means of the National Cancer Institute (NCI) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) (1R01CA122217). The authors would like to thank the children, families, and clinicians who participated in this research. We are also grateful to the site research assistants for their dedication and contribution.

Biographies

Patricia A. Marshall is Professor and Co-Director of the Center for Genetic Research Ethics and Law in the Department of Bioethics at the School of Medicine, and Professor in the Department of Anthropology, all at Case Western Reserve University, Cleveland, Ohio. She was involved in the conception and design of the qualitative methods for this study, the analysis and interpretation of data for this paper, and drafted and revised the manuscript.

Ruth V. Magtanong is completing her work for a doctoral degree in Anthropology in the Department of Anthropology at Case Western Reserve University in Cleveland, Ohio. She was a Research Assistant in the Department of Bioethics at the Cleveland Clinic, Cleveland, Ohio, during the analysis and preparation of the paper. She was directly involved in the analysis and interpretation of data and in drafting and revising the manuscript.

Angela C. Leek is the Research Assistant in the Department of Bioethics at the Cleveland Clinic. She is currently staffing the “Informed Consent in Pediatric Phase I Cancer Trials” study and was involved in authorship of the manuscript.

Sabahat Hizlan is the Data Manager in the Department of Bioethics at the Cleveland Clinic. She is currently working on the “Informed Consent in Pediatric Phase I Cancer Trials” and she was involved in the data analysis and data interpretation of the manuscript, including the random sampling of the data.

Amy Yamokoski is currently a Research Program Manager in the Center for Clinical Research and formerly the Project Director for the “Informed Consent in Pediatric Phase I Cancer Trials” study in the Department of Bioethics at Cleveland Clinic. She contributed to the conceptualization and design of the project, the interpretation of the data, the drafting and editing of the manuscript, and administrative and supervisory oversight of the research project.

Eric Kodish is Director of the Center for Ethics, Humanities and Spiritual Care at Cleveland Clinic, where he holds the F. J. O’Neill Professor and Chair of Bioethics. He is Professor of Pediatrics, Oncology and Bioethics, Lerner College of Medicine at Case Western Reserve University. He is the Principal Investigator on the NIH-funded project entitled “Informed Consent for Pediatric Phase I Cancer Trials,” and contributed to the conceptualization of the project, writing of the manuscript, and administrative oversight of the research.

References

- Agrawal M, Grady C, Fairclough DL, Meropol NJ, Maynard K, Emanuel EJ. Patients’ decisionmaking process regarding participation in phase 1 oncology research. *Journal of Clinical Oncology*. 2006; 24(27):4479–4484. [PubMed: 16983117]

- Cohen MZ, Slomka J, Pentz RD, Flamm AL, Gold D, Herbst RS, Abbruzzese JL. Phase I participants' views of quality of life and trial participation burdens. *Supportive Care in Cancer*. 2007; 15(7):885–890. [PubMed: 17252219]
- Coleman CH. Vulnerability as a regulatory category in human subject research. *Journal of Law Medicine, and Ethics*. 37(1):12–18.
- Corbin, J.; Strauss, A. *Basics of qualitative research*. Los Angeles: Sage Publications; 2008.
- Department of Health, Education, and Welfare. The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research. 1979. Retrieved from <http://ohsr.od.nih.gov/guidelines/belmont.html>
- de Vries MC, Houtlosser M, Wit JM, Engberts DP, Bresters D, Kaspers GJ, van Leeuwen E. Ethical issues at the interface of clinical care and research practice in pediatric oncology: A narrative review of parents' and physicians' experiences. *BMC Medical Ethics*. 2011; 12:18. [PubMed: 21943406]
- Finlay E, Casarett D. Making difficult discussions easier: Using prognosis to facilitate transitions to hospice. *CA: A Cancer Journal for Clinicians*. 2009; 59(4):250–263. [PubMed: 19535791]
- Glaser, BG.; Strauss, AL. *The discovery of grounded theory: Strategies for qualitative research*. Chicago: Aldine Publishing; 1967.
- Hinds PS, Pritchard M, Harper J. End-of-life research as a priority for pediatric oncology. *Journal of Pediatric Oncology Nursing*. 2004; 21(3):175–179. [PubMed: 15296049]
- Jenkins VA, Anderson JL, Fallowfield LJ. Communication and informed consent in phase I trials: A review of the literature from January 2005 to July 2009. *Supportive Care in Cancer*. 2010; 18(9): 1115–1121. [PubMed: 20204418]
- Jenkins V, Solis-Trapala I, Langridge C, Catt S, Talbot DC, Fallowfield LJ. What oncologists believe they said and what patients believe they heard: An analysis of phase 1 trial discussions. *Journal of Clinical Oncology*. 2011; 29(1):61–68. [PubMed: 21098322]
- Kass N, Taylor H, Fogarty L, Sugarman J, Goodman SN, Goodwin-Lander A, et al. Purpose and benefits of early phase cancer trials: What do oncologists say? What do patients hear? *Journal of Empirical Research on Human Research Ethics*. 2008; 3(3):57–68. [PubMed: 19385771]
- Kodish E. Pediatric ethics and early-phase childhood cancer research: Conflicted goals and the prospect of benefit. *Accountability in Research*. 2003; 10(1):17–25. [PubMed: 14552299]
- Kodish ED, Pentz RD, Noll RB, Ruccione K, Buckley J, Lange BJ. Informed consent in the children's cancer group: Results of preliminary research. *Cancer*. 1998; 82(12):2467–2481. [PubMed: 9635541]
- Koh TH, Butow PN, Coory M, Budge B, Collie LA, Whitehall J, Tattersall MH. Provision of taped conversations with neonatologists to mothers of babies in intensive care: Randomised controlled trial. *BMJ (Clinical research ed.)*. 2007; 334(7583):28.
- Miller FG, Joffe S. Benefit in phase 1 oncology trials: Therapeutic misconception or reasonable treatment option? *Clinical Trials*. 2008; 5(6):617–623. [PubMed: 19029210]
- Morse, JM. Strategies for sampling. In: Morse, JM., editor. *Qualitative nursing research: A contemporary dialogue*. Newbury Park, CA: Sage Publications; 1991. p. 117–131.
- Simon C, Zyzanski SJ, Eder M, Raiz P, Kodish ED, Siminoff LA. Groups potentially at risk for making poorly informed decisions about entry into clinical trials for childhood cancer. *Journal of Clinical Oncology*. 2003; 21(11):2173–2178. [PubMed: 12775743]
- Sulmasy DP, Astrow AB, He MK, Seils DM, Meropol NJ, Micco E, Weinfurt KP. The culture of faith and hope: Patients' justifications for their high estimations of expected therapeutic benefit when enrolling in early phase oncology trials. *Cancer*. 2010; 116(15):3702–3711. [PubMed: 20564120]
- Yap TY, Yamokoski AD, Hizlan S, Zyzanski SJ, Angiolillo AL, Rheingold SR, Baker JN, Kodish ED. Informed consent for pediatric phase 1 cancer trials: Physicians' perspectives. *Cancer*. 2010; 116(13):3244–3250. [PubMed: 20564626]
- Yap TY, Yamokoski A, Noll R, Drotar D, Zyzanski S, Kodish E. A physician-directed intervention: Teaching and measuring better informed consent. *Academic Medicine*. 2009; 84(8):1036–1042. [PubMed: 19638769]

FIGURE 1.
Framework for Negotiating Micro-Decisions in Informed Consent.

TABLE 1

Patient (N=16) and Parent (N=16) Characteristics.

Patients		n	%
Gender	Male	11	69
	Female	5	31
Age, years	Mean	13.25	
	Standard Deviation	4.70	
	Range	5–21	
Age groups, years	5–9	4	25
	10–14	6	37.5
	15–19	6	37.5
Parents		n	%
Interviewed Parent	Mother	10	62.5
	Father	6	37.5
Age, years	Mean	42.06	
	Standard Deviation	8.95	
	Range	28–66	
Age groups, years	25–34	3	19
	35–44	7	44
	45–54	5	31
	55	1	6
Education	Some high school	1	6
	Completed high school	2	13
	Some college	5	31
	College graduate	7	44
	Postgraduate level	1	6
Ethnicity	Asian/Asian American	1	6
	African American/Black	1	6
	White (Origins in Europe)	14	88
ISP* (1=highest)	1–1	4	25
	3	6	37.5
	4–5	6	37.5
Has your child ever before participated in a research study for the treatment of his/her cancer?	No	3	19
	Yes	13	81
Has your child participated in a Phase 1 study?	No	8	50
	Yes	4	25

Patients		
Can't recall	1	6
Missing	3	19

* Hollingshead Index of Social Position.

Socioeconomic status was measured by the ISP, which assigns socioeconomic status using education and occupation. On this scale of 1 to 5, a lower ISP score represents a higher socioeconomic status.

TABLE 2

Micro-Decision Domains, Categories, Issues in Negotiation Process during ICCs (N=16 ICCs).

Micro-Decision Domain	Micro-Decision Category	Micro-Decision Issues Discussed*	# of ICCs n (%)
Drug Logic and Logistics	Drug efficacy	How drug impacts cancer	10 (63)
		Reasons for offering trial	
	Drug delivery	Method of delivery	10 (63)
		Timing of delivery	
	Monitoring toxicity	Reducing side effects	10 (63)
		Quality of life	
		Preventing infections	
	Treatment location	Hospital	8 (50)
		Out-patient clinic	
		Home	
Scheduling Drug Administration	Dates/Time	Distance to travel	6 (38)
		Duration of procedure	
		Family and social obligations	
	Daily living	School and work activities	7 (44)
		Sports and recreational activities	
		Family relationships	

* The average number of micro-decisions discussed in an ICC is 5 (range 2–8).