Hope and Persuasion by Physicians During Informed Consent

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ABSTRACT

Purpose

To describe hopeful and persuasive messages communicated by physicians during informed consent for phase I trials and examine whether such communication is associated with physician and parent ratings of the likelihood of benefit, physician and parent ratings of the strength of the physician's recommendation to enroll, parent ratings of control, and parent ratings of perceived pressure.

Patients and Methods

Participants were children with cancer ($n = 85$) who were offered a phase I trial along with their parents and physicians. Informed consent conferences (ICCs) were audiotaped and coded for physician communication of hope and persuasion. Parents completed an interview ($n = 60$), and physicians completed a case-specific questionnaire.

Results

The most frequent hopeful statements related to expectations of positive outcomes and provision of options. Physicians failed to mention no treatment and/or palliative care as options in 68% of ICCs and that the disease was incurable in 85% of ICCs. When physicians mentioned no treatment and/or palliative care as options, both physicians and parents rated the physician's strength of recommendation to enroll in the trial lower.

Conclusion

Hopes and goals other than cure or longer life were infrequently mentioned, and a minority of physicians communicated that the disease was incurable and that no treatment and/or palliative care were options. These findings are of concern, given the low likelihood of medical benefit from phase I trials. Physicians have an important role to play in helping families develop alternative goals when no curative options remain.

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INTRODUCTION

Phase I studies are designed to test the safety profile of novel agents and typically enroll patients for whom other treatments have failed. Ethical concerns have been raised about adult and pediatric phase I trials, including questions about vulnerability, the burden of study participation, and whether patients and families understand the purpose and low likelihood of benefit.¹⁻³ Because the offer of a phase I trial comes when the options for cancer-directed interventions are limited, the situation provides an opportunity for patients and families to reconsider their hopes and goals moving forward (eg, pain management, time with family, being cared for and supported⁴⁻⁸). At the same time, parents may selectively attend to hopeful messages to maintain their positive outlook^{9,10} and may be susceptible to communication that reinforces their hopes regarding the trial. Physi-

cians also have hopes for the patient, and conversations about poor prognosis and end-of-life options can be incredibly challenging.^{6,11,12}

For this study, informed consent conferences (ICCs) about phase I research enrollment in pediatric cancer were observed. The present analysis focused on hopeful and persuasive communication from physicians to patients and their parents, employing qualitative and quantitative approaches. The goals for the analysis were to describe physician communication of hope, persuasion, realism, and alleviate pressure; determine whether patient or physician characteristics are associated with physician communication; and test associations of physician communication with physician and parent ratings of the likelihood of benefit of the trial, physician and parent ratings of the strength of the physician's recommendation to enroll, parent ratings of control after the ICC, and parent ratings of perceived pressure to enroll.

PATIENTS AND METHODS

Recruitment and Procedures

Participants, recruited from six children's hospitals in the United States, were parents and their children who were offered a pediatric phase I trial between June 2008 and June 2011.¹³ The study was approved by the institutional review board at each site.

Parents and patients age 18 to 21 years provided written informed consent. Verbal or written assent, depending on the institution, was obtained for children age 7 to 17 years. The ICCs for the trial were observed and audiotaped. Afterward, the parent who participated most during the ICC was invited to complete an interview. The physician was asked to complete a case-specific questionnaire. Audiotapes of the ICCs were transcribed, anonymized, and uploaded into NVivo 10 (QSR International, Doncaster, Australia) for coding and analysis.

Coding of ICCs and Interrater Reliability

Three of the authors (V.A.M., M.C., and A.C.L.) followed common methods for developing a coding scheme for qualitative data.^{14,15} The final coding structure included four primary codes: Hope, Realism, Persuasion, and Alleviate Pressure. Hope and Persuasion had subcodes to further differentiate the codes conceptually (Table 1). Realism and Alleviate Pressure were more uniform and did not require subcodes. Seventeen transcripts (20%) were double-coded for interrater reliability. Intraclass correlation coefficients, based on frequencies of each primary code in each transcript, ranged from 0.70 to 0.93, indicating excellent interrater reliability.¹⁶

Measures

Parent interview. A subset of parents consented to complete the interview ($n = 60$). The present analysis included data from four items. The item assessing likelihood of medical benefit asked for a response as a percentage. The items assessing strength of recommendation, control, and pressure were rated on a visual analog scale; higher scores indicated greater strength of recommendation, more control, and more pressure.

Case-specific clinician questionnaire. Physicians were invited to complete the case-specific clinician questionnaire for each ICC that they conducted. The present analysis included data from three items. The two items assessing likelihood of benefit asked for a response as a percentage. The item assessing strength of recommendation was rated on a visual analog scale, with higher scores indicating greater strength of recommendation.

Data Analysis

Descriptive information related to each of the codes was calculated, including the mean frequency of each primary code and the percentage of ICCs in which each code and subcode occurred. Illustrative quotes are in Table 1. To understand the balance of Hope to Realism codes and Persuasion to Alleviate Pressure codes, frequency ratios were calculated for each ICC and averaged. For the quantitative analyses examining relationships among the four primary codes, code frequencies were first divided by the duration of the ICC to account for the fact that code frequencies were higher in longer ICCs. Spearman correlations and the Mann-Whitney U test were used to test associations of Hope, Realism, Persuasion, and Alleviate Pressure with patient and physician characteristics, physician and parent ratings of the likelihood of benefit and the strength of the physician's recommendation to enroll, and parent ratings of control after the ICC and perceived pressure to participate. Patient and physician characteristics that we examined included patient age; whether it was the physician's first interaction with the patient/family; whether the patient was referred from another institution; and physician age, sex, years in practice, and role (attending v fellow).

ducted by 34 different physicians. The average number of ICCs conducted by each physician was 2.50 (standard deviation [SD], 2.23; range, 1-9). Thirty of the participating physicians provided descriptive information about themselves (Table 3).

Description of Physician Communication

Descriptive data for the parent interview and case-specific clinician questionnaire are in Table 4.

Hope. The Hope code included physician statements indicating hope or expectation that the phase I drug would delay cancer progression, lengthen life, or cure the disease. This code also included general hopes for positive outcomes, indication that they would keep fighting the disease, identification of goals, and indication that there were multiple phase I options or other options besides the phase I trial (either currently or if the phase I drug did not work). In addition, the Hope code included the physician stating that the patient had tolerated or responded well to similar drugs in the past and that the patient is currently doing well with respect to symptoms and/or stable disease. Hopes and goals other than cure or longer life, such as more time with family or a pain-free death, were infrequently mentioned.

The most frequent Hope statements were expectation of positive outcomes (89% of ICCs) and options (74% of ICCs; Table 1). The mean number of Hope statements per ICC was 7.60 (SD, 5.38; range = 0-28). The options subcode was reviewed to determine whether or not the physician indicated that no treatment and/or palliative/hospice care were options. Physicians failed to mention these in 68% of ICCs ($n = 58$). Physicians used the words "palliative" or "palliate" or "hospice" in only eight ICCs.

Realism. Realism encompassed comments from the physician indicating low or zero probability of benefit from the trial, uncertainty regarding whether the study drug would work, that the study drug may cause intolerable adverse events, that there are no curative options, lack of options in general, that the disease is progressing, difficult to treat/aggressive or incurable, and that past and standard treatments given to the patient had not worked or had not been tolerated. The mean number of Realism statements per ICC was 3.13 (SD, 2.92; range, 0-15). The Realism code was reviewed to determine whether or not the physician explicitly stated that there were no curative options (or that the child had incurable disease). This type of comment was present in 15% of ICCs ($n = 13$). In other words, in 85% of ICCs, physicians failed to mention that there were no curative options for the child's cancer.

Ratio of Hope to Realism. The mean ratio of Hope to Realism statements was 3.15 (SD, 3.88; range, 0-28), indicating that physicians made approximately three hopeful statements for every realistic statement.

Persuasion. Persuasion consisted of comments that potentially could influence patients and families to enroll onto the trial or in the pharmacokinetic portion of the trial. As such, there was not necessarily intent to persuade by the physician. This code included statements that the trial was the best or only option, that a decision needed to be made urgently or that spots on the trial were scarce, a recommendation by the physician to enroll, comments about altruism, suggesting that other patients on the trial had responded to the study drug, and comments that minimized or attempted to alleviate potential burdens of participation (eg, logistics, time commitment, adverse events). The Persuasion code was also applied when the physician used language to convey excitement about the trial. The mean number of Persuasion

RESULTS

Participants

Eighty-five ICCs were observed.¹³ Demographic, illness, and ICC descriptive information is listed in Table 2. The 85 ICCs were con-

Table 1. Illustrative Quotes and Percentage of ICCs in Which Code Occurred

Code	%	Selected Physician Quote
Hope	99	
Positive outcomes	89	<p>But we also carry with us the hope, although it is not the implicit part of the study, but we carry with it the hope that this may help her. That is not the expectation of starting her on the drug, but it's my deep down hope, and I'm sure it's yours as well that, you know, this could benefit [patient's name], keep her feeling good.</p> <p>I'll be disappointed if we don't see response. You know . . . I mean . . . we are . . . we are very hopeful that this is going to be a drug that will . . . um . . . eliminate tumor and . . . and I mean . . . I don't wanna give you false hope but we certainly . . . all of the evidence points to the fact that for patients whose tumors have this mutation, this should kill those cells. It should eliminate them.</p> <p>The real important thing I think, uh, for uh, fathers and mothers is, um, to um, remember that, uh, we're exposing her to these risks because we expect it to help. . . . I'm cautiously optimistic that this is going to help her and I'm very hopeful that in six weeks those scans are going to be better. Is it possible that this could clear her scans and clear her bone marrow? Yeah, it's possible.</p>
Staying positive	23	I think that, you know, you're obviously trying to see the cup half-full and I agree with you.
Keep fighting	8	<p>On the other hand, like, I think one of the reasons you have been thinking about this stuff is that you don't want to leave a stone unturned and that if things don't go the way that we wish they would, you can look back and say, "I tried."</p> <p>We felt that you guys still want to fight this, okay? And we both agreed that [patient's name] is still in good shape, that if you guys want to do it, it's worth trying.</p>
Goals	25	<p>We want . . . our goal is to have [patient's name] a 30-, 80-year-old, happy, healthy young man.</p> <p>That, like, we will preference doing things that make you happy and make your family happy and make, um . . . like, the whole point of this for me is giving you as much quality good time with your family and friends and being out of the hospital as possible.</p>
Options	74	<p>The thing that we find so frustrating as a team is to have a patient and come to them empty-handed and say "I'm sorry. I just don't have anything for you." And I think you are in sort of the opposite . . . you're in sort of . . . you know . . . you're in the candy store and you get to choose which you want. I think all of these options . . . a sane person in their right mind could take and we, as medical professionals, are very geared towards the clinical trials or [name of institution] wouldn't be [name of institution] . . . you know . . . that's our job is to provide that option to you.</p> <p>So those are kind of the treatment options. The other option, and I'll bring it up only because some people are kind of afraid to ask, is to say, well, maybe we should just do treatment for your symptoms, treating your pain, but not medicines to treat the cancer. 'Cause you did a whole bunch of chemotherapy and radiation already, and some people are afraid to ask that question, because they don't know what'll happen. Well, you certainly won't have any symptoms from the treatment, but we expect the cancer is gonna start to get worse again. Worse in the bones where you got radiation maybe, or worse in the bones where you haven't got any radiation. [patient: Mm-hmm.] And we know what will happen with that, so the cancer will keep getting worse. But for some people that's not a bad choice, because they just grow tired of the chemotherapy, they don't want to travel [Dad: Mm-hmm.] a long way to get treated. I'm not saying that's the right thing to do for you, 'cause you've come a long way not to go back home and not get treated.</p> <p>Um . . . and I think that there are several choices about what to do to treat it. There are people who would say "I don't want treatment. I'm tired of being on treatment," and that's okay.</p>
Reminder of past successes	7	<p>Again, it's hard, because we don't know and we have very limited experience, but my hope is that his experience on this will be very similar to his experience on the antibody study . . . went straightforward, also well tolerated. You know that's where the hope . . .</p> <p>And I think that's what we had kinda decided on was to do the gemcitabine docetaxel. I think that's pretty reasonable. You were on that for a really long time. We stopped it, not because it wasn't working, but because I told you you could stop it, all right?</p>
Child doing well	14	<p>Everything there is completely stable and there's no . . . the tumor hasn't started to grow back. There is no evidence that there is tumor there. Everything looks, you know, your, your lung's good and you don't have any infection there. So that's actually, another good thing, right?</p> <p>And she really has done so much better than any other child I have seen with a brainstem glioma, I have got to say. I have never seen someone who had so few symptoms.</p>
Realism	78	<p>And then again we don't know; I can't even give you percentages for how well it will work. It's just we don't know. It might not work at all.</p> <p>And I think that the other thing is what you said earlier, too, is that, well, I think from the time we've met we've been brokenhearted with the tumor she has, and I think you've known from the beginning that she has an incurable disease.</p> <p>So we're talking about situations where, in many ways, we know we don't have any really good options that have proven benefit.</p> <p>I think that, um, right now you have a disease that we cannot cure and we have tried. We have given it a good fight and there is nothing that you have done wrong to make that happen, obviously; you certainly didn't make yourself get it. No one made you get it. Um, we have given it a good go with as many chemotherapies as we have, and like I said, if I had a better drug to give you right now, I obviously would give it to you.</p> <p>If we're not going to do anything about it, it will kill him. Even with a phase I study, it is unfortunately still going to kill him . . .</p>
Persuasion	93	
Words to describe trial	43	<p>We don't have as much experience with [patient's name] tumor, but one thing that [physician's name] and I are excited about is there's a class of drugs that interfere with cell division, so it's called mitosis.</p> <p>So this whole thing of molecularly targeted therapy . . . it's biologically based . . . it's very rational and we're really into it and excited about it.</p> <p>But this is a drug that has shown a lot of promise in the laboratory because the way it works is it works at the level of the receptors on the tumor cells that are used to help the tumor cells grow out of control of the rest of the body.</p>
(continued on following page)		

Table 1. Illustrative Quotes and Percentage of ICCs in Which Code Occurred (continued)

Code	%	Selected Physician Quote
No other option	19	Um, again, you know, when you are in a place where you don't have a lot of options, something that works in a test tube is probably worth trying. As long as everybody understands the pros and cons. So I think it's certainly something worth trying, and you know he's at a point, because he's had both CCNU and temozolomide, that there aren't any other standard chemotherapy drugs that have any proven benefit, so we're sort of at the point where we're using new drugs.
Urgency	25	After this week, if we lose this spot, then it may be another month or two before we can even reconsider, okay? Yeah, that can happen because there's . . . there's about 21 hospitals around the country that are part of this study, actually it is a little bit more than that for this study, and um, they are all looking to get a spot for the same, you know, patients like you who they have, and if a spot's available they often are taken up pretty quickly. So it's quite possible that if you changed your mind and then changed your mind again twenty-four hours later the spot wouldn't be available.
Altruism	51	We don't know, right, so basically, so one of the reasons, if you're interested in participating in the study, one of the big reasons to do it is to help us learn more about the drug to help, even if it doesn't work for you, it would help other children in the future 'cause we're going to learn more about the side effects and the toxicity and the best dose of this drug to use. We understand that some people will say "Okay, if I can answer that question, even if it's not for me, for somebody else, I want to do it," and somebody else says "You know you need to be selfish right now. No, I don't want to do that," that's fine. Most people I think want to do it because they want to, like, help all of us learn something about this. I had one mom whose kid went on no less than I think 5 or 6 phase I studies who insisted on doing the PK. [Laughter.] But really she's done so many and the mom was just insistent on doing it, because she felt like it was important for something good to come out of something bad.
Others responding/ tolerating study drug	29	Patients who have mutant <i>ALK</i> in their lung tumors have shown dramatic responses to this drug. So . . . a lot of enthusiasm. There have been kids who have been on this drug now for a long time, like close to a year. Um, a couple kids who have been on it for right around a year who have had stable disease. So the first patient, he got two courses. After the first course, his disease was stable.
Child responded to similar drug in past	9	Unlike many other experimental trials that is of a drug that hasn't been tried before, this is a drug that she's had in the past and has worked for her and is a better form of it, we think. So one of the reasons we like this study for [patient's name] is because it includes some of the drugs that he got initially.
Implied lack of choice	21	But I'm going to think that the reason you came today was 'cause you want to go for it. And [patient's name], you know we talked about this before, I think you're old enough and understand this well enough, given everything that you've been through, to give us your signature to let us know that you're okay to start this medicine. Okay, but the reason that people like yourselves participate in these studies is because it gives you . . . this is a possibility. You've really exhausted all your other options.
Minimize logistics or side effects	62	One of the medicines apparently tastes pretty bad. I know you can do it though . . . That is something to tell you, but it should not influence your choice. It's in your mind, 'cause you think that there's a pill and it's hard to swallow, but you really, in real life, you can actually swallow much bigger pieces of food than a pill. 'Cause ultimately this is about you guys being with her and her feeling good as often as possible. So we will sort out any scheduling things so your visits are the minimal that they can be. So then nausea is something that . . . you know . . . is an expected side effect and many patients get . . . many patients find it manageable . . . many patients have it in their first cycle and then it sort of goes away.
Physician recommendation	29	Um . . . but because the risks of this medicine, in our opinion, are relatively low and the benefit, if this is a good drug for her, could be extremely high, we think this is an investigational drug that is . . . we recommend very strongly, and I'd ask you to consider very strongly. So there are alternatives, um, but in our opinion, um, for where [patient's name] is in her story with this disease right now, this makes a lot of sense and I'm glad that the contract is signed or will be signed or . . . So, I think it would be a very good idea to start some kind of experimental therapy to try to see if we can control this disease. It's optional, but this is one of the things . . . in fact, I'd like to strongly advise my patients. I've never seen someone say "no" [regarding the PK portion of the study].
Alleviate pressure	78	I say it's optional, because it's not your treatment [referring to the PK portion of the study]. If you were to tell me, "Look, if you're not 100% certain, then I'd rather not do something. I'd rather not start a new treatment. I'd rather, given my clinical progression, start on some steroids and see how I do," then I'd say to you, "Okay, I'm okay with that." If you know you really want to do it, we will do it. If you're not sure, you probably shouldn't do it. But it is considered research, and it's completely your choice. I think that's something that's really important, is saying . . . sometimes it feels like when you sign this, it's like signing a contract, and I'm the study doctor and I'm gonna make you do this. [Dad chuckles.] That's not the way it is, you can always back out. And if you back out, then we just say, okay, well, let's sit down and talk about what your options are now. Um, if you are like, "This is terrible and I am done." Then that is it, you know? For me, that is the end. That is the end of the study. Okay? And that will neither affect our relationship, change your treatment at [name of institution], you know, change anything. And if you don't want to do it, it's not going to change anything either. Now if you withdraw from the study, there are no consequences. We'd try to talk to you out of it, we'd understand why, but if you insist, we can seek other options, okay?

Abbreviations: CCNU, chloroethyl-cyclohexyl-nitrosourea; ICC, informed consent conference; PK, pharmacokinetics.

Table 2. Patient and ICC Characteristics (n = 85)

Characteristic	No.	%
Age, years		
1-6	19	22
7-13	34	40
14-17	17	20
18-21	15	18
Mean	11.34	
SD	5.47	
Range	1-21	
Child sex (male)	54	64
Cancer type		
Brain/CNS	28	33
Bone or soft tissue	26	31
Neuroblastoma	17	20
Leukemia	7	8
Other	7	8
Time from diagnosis to ICC, years		
Mean	2.86	
SD	2.37	
Range	0.12-12.46	
First interaction with physician	13	15
Referred from another institution	36	42
Duration of ICC, minutes		
Mean	44.53	
SD	19.95	
Range	15-128	
Enrolled onto phase I trial	81	95

Abbreviations: ICC, informed consent conference, SD, standard deviation.

statements per ICC was 6.21 (SD, 4.65; range, 0-18). The most frequent Persuasion statements were those that minimized logistics (62% of ICCs), those of altruism (51% of ICCs), and words used to describe trial (43% of ICCs; Table 1).

Alleviate Pressure. Alleviate Pressure was defined as comments that potentially could alleviate pressure to enroll. Comments included those indicating that it is the patient's/parent's decision, that the pharmacokinetic portion of the study was optional, that there was no pressure to enroll, that they could change their minds at any time, that no one would be angry if they did not enroll, and that the patient would continue to receive care regardless of the decision. The mean

Table 3. Physician Characteristics (n = 30)

Characteristic	No.	%
Age, years		
Mean	43.60	
SD	6.65	
Range	29-61	
Sex (male)	14	47
Time in practice, years		
Mean	13.71	
SD	7.84	
Range	1-32	
Clinical role		
Attending	27	90
Fellow	3	10

Abbreviation: SD, standard deviation.

Table 4. Descriptive Statistics for Parent Interview and Case-Specific Clinician Questionnaire

Variable	Mean	SD	Range
Parent interview			
Likelihood that child will get medical benefit from phase I trial, %	50.67	35.12	0-100
Strength of physician's recommendation to participate in phase I study, from 0 ("not very strongly") to 10 ("very strongly")	5.57	3.59	0-10
Perception of control as a result of information provided about the phase I trial, from 0 ("less in control") to 10 ("more in control")	6.45	2.72	0-10
Perceived pressure to participate in phase I study, from 0 ("no pressure") to 10 ("much pressure")	1.55	2.52	0-10
Case-specific clinician questionnaire			
Likelihood that child will get medical benefit from phase I trial, %	22.55	20.86	0-95
Likelihood that child will get psychological benefit from phase I trial	53.00	31.38	0-100
Strength of physician's recommendation to participate in phase I study, from 0 ("not very strongly") to 10 ("very strongly")	6.20	2.27	0-10

Abbreviation: SD, standard deviation.

number of Alleviate Pressure statements per ICC was 3.36 (SD, 3.30; range, 0-14).

Ratio of Persuasion to Alleviate Pressure. The mean ratio of Persuasion to Alleviate Pressure was 0.88 (SD, 1.29; range, 0-8), indicating that there was an almost one to one correspondence between Persuasion and Alleviate Pressure statements.

Associations between primary codes. Realism was positively associated with Alleviate Pressure ($r = 0.23$; $P = .034$) and Persuasion ($r = 0.37$; $P = .001$). Hope was not associated with Alleviate Pressure or Persuasion. Hope and Realism were not associated with one another, nor were Alleviate Pressure and Persuasion.

Associations of Physician Communication With Patient and Physician Characteristics

Physician age was inversely associated with Alleviate Pressure ($r = -.26$; $P = .02$). Physician years in practice were inversely associated with Alleviate Pressure ($r = -.28$; $P = .017$) and Hope ($r = -.28$; $P = .016$). Male physicians expressed more Realism (Mann-Whitney U, 519.50; $P = .015$) and Alleviate Pressure (Mann-Whitney U, 565.00; $P = .049$) compared with female physicians. Physician communication was not associated with patient age, whether it was the physician's first interaction with the patient/family, whether the patient was referred from another institution, or whether the physician was an attending versus a fellow.

Associations of Physician Communication With Interview and Questionnaire Items

Hope and Persuasion were not significantly associated with the interview/questionnaire items. Realism was inversely associated with parent ratings of control ($r = -.27$; $P = .047$). Alleviate Pressure was inversely associated with physician ratings of psychological benefit ($r = -.33$; $P = .004$).

When no treatment and/or palliative care were mentioned as options, physician ratings of the likelihood of psychological benefit

were lower (Mann-Whitney U, 356.00; $P = .002$), physician ratings of strength of recommendation to enroll were lower (Mann-Whitney U, 334.50; $P < .001$), and parent ratings of the physician's strength of recommendation to enroll were lower (Mann-Whitney U, 213.50; $P = .013$) compared with when no treatment and/or palliative care were not mentioned as options.

DISCUSSION

Therapeutic effect is not the primary end point of phase I studies, and the chances of direct medical benefit are low.¹⁷⁻¹⁹ However, in the majority of ICCs (85%), physicians failed to mention that there were no curative options for the child's cancer. In 68% of ICCs, physicians did not indicate that no treatment and/or palliative care were options. There are several reasons why physicians may not fully disclose prognostic information, including their own estimation of benefit of the trial,¹¹ personal hopes for the patient, effort to support patient and family hopes,²⁰ or concern that such disclosure will cause distress.¹² Our findings are consistent with prior research in adult settings, showing that the majority of oncologists reinforce hopes with respect to the therapeutic effects of phase I trials.^{21,22} However, communication that is falsely reassuring may lead patients and parents to make decisions they might not have made otherwise,³ such as accepting more toxic approaches.²³ This communication pattern may also cause distress or resentment when it becomes clear that the hoped-for goal cannot be achieved.

Lack of recognition on the part of physicians and/or families that cure is unlikely makes it less likely that palliative care will be incorporated into the treatment plan.²³ When hospice care is discussed earlier, parents are more likely to describe their children as calm and peaceful in the last month of life.²⁴ The vast majority of children with cancer who are offered phase I studies will die as a result of their disease. For example, 6 months after recruitment for this study was complete, 76% of the patient participants ($n = 65$) had died, and the mean length of time between the ICC and date of death was 254 days (SD, 229.3; 17-981).¹³ Failure to mention palliative care at a key point in decision making is concerning, yet not surprising, given that inadequate palliation is frequent in the last month of life for children with cancer.²⁴ Our analyses indicated that when no treatment and/or palliative care were mentioned as options, parents and physicians both reported that the physician's strength of recommendation to enroll onto the trial was lower. Communication that allows for the possibility of palliative care may pave the way for more effective palliative care as the disease progresses. Furthermore, given that informed consent requires disclosure of risks, benefits, and alternatives to research participation,²⁵ palliative care should be mentioned in this context.

Recognition that goals other than cure were worth pursuing was infrequent. Hope theory suggests that when hoped-for goals are unattainable (eg, cure), patients and families may become especially distressed if there are no other goals (eg, quality time with family; pain control) to work toward.²⁶ Individuals with a terminal illness and their families may have more positive emotions if they develop realistic goals, even if those goals occur in conjunction with the hope for prolonged life.²⁷ In the emotional context of relapse and/or cancer progression, patients and their families may need explicit guidance and support to develop and discuss alternative goals when few curative options remain.^{4,20,28}

The mean ratio of hopeful to realistic communication (approximately 3 to 1) indicates that ICCs were more hopeful than not. As expected, the frequencies of hopeful and realistic statements were not associated. Hopeful communication and realistic communication are not necessarily on opposite ends of the same continuum. Parents of children with cancer and bereaved parents have reported that they want their providers to communicate a balance of hope and realism,^{10,29} but providers report that achieving such a balance is a challenge.^{6,11,12} Not surprisingly, realistic communication was associated with lower parental ratings of control. Knowledge that options for further cancer-directed care are limited and that the phase I trial is unlikely to provide a cure is distressing and can signal an important shift in the disease trajectory.

The themes of persuasion that were present in the pediatric phase I ICCs were similar to those in the literature related to adult participants.³⁰ The high frequency of persuasion is concerning, given that the majority of physicians who conduct phase I pediatric oncology ICCs reported that they do not attempt to influence the decision to enroll.¹¹ It is possible that physicians are not consciously aware of more subtle forms of persuasion in their communication with patients and families. For example, mentioning other patients who are responding well to the study drug gives the impression that the likelihood of direct medical benefit is higher than it actually is. Although parents and patients may desire and/or ask for this information,³¹ physicians should be honest in their approach and indicate that most patients do not respond.

The findings should be interpreted in light of several limitations. The majority of participants agreed to enroll onto the phase I trial, so the findings may not be generalizable to ICCs of those who do not enroll. The sample may be biased in that physicians may have been more likely to identify families for this study who were higher functioning or struggling less with decision making compared with other families. It is possible that conversations about prognosis and other options occurred outside of the ICCs that were the focus of this study. In addition, our sample may overrepresent patients and families who had already decided to participate in the phase I trial before the formal ICC. Physician knowledge of this may have impacted communication during the ICC. Furthermore, the data were not independent, given that individual physicians conducted more than one ICC; future research should be designed to account for nonindependence. Finally, our assessment did not allow for an understanding of the intent of physician communication and the long-term effects of such communication on patients and families.

The findings raise important questions for future research. First, research is needed to explain the variability in how physicians describe the phase I trial and understand relationships between the content ("what") and process ("how") of communication during ICCs. Second, prospective research is needed to understand how decision making unfolds from the phase I decision to consideration and implementation of palliative care and how physician communication shapes this path. Although parents and patients may pursue additional cancer-directed interventions, earlier discussion of poor prognosis and palliative care paves the way for effective concurrent palliation or downstream hospice care.²³ Finally, interventions are needed to improve communication regarding pediatric phase I cancer trials. Strategies are needed to reduce physicians' unbalanced presentations of the purpose and benefits of phase I trials. Pediatric oncologists will likely embrace education regarding the subtle and unintentional ways in which their communication may be persuasive. Physicians have an

important role to play in helping families develop and discuss their goals when no curative options remain. Tempering hope with realism is one way to be compassionate with patients and families while supporting informed decision making at the end of life.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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