original report

Duality of Purpose: Participant and Parent Understanding of the Purpose of Genomic Tumor Profiling Research Among Children and Young Adults With Solid Tumors

abstract

Purpose Increasing use of genomic tumor profiling may blur the line between research and clinical care. We aimed to describe perspectives of research participants about the purpose of genomic tumor profiling research in pediatric oncology.

Methods We surveyed 45 participants (response rate, 85%) in a pilot study of genomic profiling in pediatric solid tumors at four academic cancer centers after the return of sequencing results. We defined understanding according to a one-item (basic) definition (recognition that the primary purpose was not to improve the patient's treatment) and a four-item (comprehensive) definition (primary purpose was not to improve patient's treatment; primary purpose was to improve treatment of future patients; there may not be direct medical benefit; most likely result of participation was not increased likelihood of cure).

Results Sixty-eight percent of respondents (30 of 44 respondents) demonstrated basic understanding of the study purpose; 55% (24 of 44 respondents) demonstrated comprehensive understanding. Understanding was more frequently seen in those with higher education and greater genetic knowledge according to basic (81% *v* 50% [*P* = .05]; and 82% *v* 46% [*P* = .03], respectively) and comprehensive (73% *v* 28% [*P* = .01]; 71% *v* 23% [*P* = .01]) definitions. Ninety-three percent of respondents who believed the primary purpose was to improve the patient's care simultaneously stated that the research also aimed to benefit future patients.

Conclusion Most participants in pediatric tumor profiling research understand that the primary goal of this research is to improve care for future patients, but many express dual goals when they participate in sequencing research. Some populations demonstrate increased rates of misunderstanding. Nuanced participant views suggest that additional work is needed to assess and improve participant understanding, particularly as tumor sequencing moves beyond research and into clinical practice.

Jonathan M. Marron
Angel M. Cronin
Steven G. DuBois
Julia Glade-Bender
AeRang Kim
Brian D. Crompton
Stephanie C. Meyer
Katherine A. Janeway
Jennifer W. Mack

Author affiliations and support information (if applicable) appear at the end of this article.

Corresponding author: Jonathan M. Marron, MD, MPH, 450 Brookline Ave, Boston, MA 02215; Twitter: @JonMarronMD @ChildCancerCare, @HMSbioethics; e-mail: jonathan_marron@dfci.harvard.edu.

INTRODUCTION

Parents of children with cancer[1,2] and adults with cancer[3-5] often fail to understand the purpose of clinical trials in which they participate. Understanding the distinction between the goals of research and clinical care is of particular importance in early-phase oncology trials, in which response rates approximate 10%.[6,7] Up to 60% of research participants demonstrate evidence of therapeutic misconception,[3,4,8,9] the belief that the primary purpose of research is therapeutic in nature rather than acquisition of generalizable knowledge.[10,11]

The precision medicine era invites new exploration of these findings. Paradigm-shifting successes with targeted treatments[12-15] highlight the potential of a precision approach to cancer care, as have reports of extraordinary responders

among adults[16,17] and children.[17-20] Although advances in targeted therapeutics generate great excitement, they may also blur the line between research and clinical care.[21,22] Young adult patients and parents of children with cancer have high hopes/expectations for tumor sequencing,[23,24] though only a minority experience clinical benefit.[25-29] This mirrors findings among adult patients with cancer[30-33] and highlights the need for a deeper understanding of the tumor profiling consent process. Although recent work has described genomic knowledge in parents and young adult cancer survivors,[23] we know little about how patients and parents who undergo sequencing perceive the role of tumor sequencing research or how they conceptualize the balance between research and clinical care in the era of precision cancer medicine.

To better understand patient/parent perceptions of these complex concepts, we queried beliefs of participants in a study that involved molecular profiling of pediatric solid tumor samples about the primary purpose of such research.

KEY POINTS

Key Objective

How well do participants in a pediatric genomic tumor profiling research study understand the purpose of participation in such research?

Knowledge Generated

Most participants recognized that the purpose of such research is to benefit future patients, but many participants demonstrated some degree of misunderstanding about the purpose of this research, and some subgroups demonstrated increased rates of misunderstanding. Furthermore, many participants simultaneously identified dual purposes for genomic tumor profiling research in pediatric oncology.

Relevance

Consenting clinicians should query and explore participant goals during presequencing counseling to identify both (1) those who do not recognize that the primary purpose of research sequencing is to generate knowledge to help future patients and (2) those who report dual purposes for this research. Additional work is necessary to better understand the perspectives and motivations of those who express this duality and to develop and test interventions to improve equitable understanding of the purpose of genomic tumor profiling research in pediatric oncology.

METHODS

We surveyed consenting participants in the iCat (Individualized Cancer Therapy) pilot study of genomic profiling in children with relapsed, recurrent, and high-risk solid tumors (ClinicalTrials.gov identifier: NCT01853345).[25] Participants were approached at Dana-Farber/Boston Children's Cancer and Blood Disorders Center (Boston, MA), University of California at San Francisco (San Francisco, CA), Columbia University Medical Center (New York, NY), and Children's National Medical Center (Washington, DC). The study was approved by the institutional review board of all participating institutions.

Individualized Cancer Therapy Study

iCat study procedures have been reported previously.[25] All patients receiving care at participating institutions were eligible for enrollment if they were age 30 years or younger at enrollment and had a recurrent, refractory, or high-risk (expected likelihood of cure < 25%) extracranial solid tumor with sufficient tumor for submission. The study consent document described the purpose of the study as follows: "to determine how often the panel of experts can [use tumor sequencing results to] make an individual treatment recommendation" and to use this information to "help future patients with cancer." Consent discussions were not standardized, nor were data collected on the content of these discussions.

Enrolled participants underwent tumor profiling via targeted next-generation sequencing and copy number assessment or a Sequenom assay. A multidisciplinary expert panel reviewed profiling results and used applicable literature to identify results with potential therapeutic implications. A letter was sent to the treating oncologist that identified such actionable results along with variants that suggested a potential change in diagnosis or possible cancer predisposition syndrome. An iCat recommendation was provided for participants who had one or more actionable

Table 1. Survey Items for Assessment of Participant Understanding of the Purpose of Genomic Profiling Research in Pediatric Oncology

Question Stem	Answer Choice		
The main reason this study was done was to improve the treatment of myself/my child.	Agree	Unsure*†	Disagree*
The main reason this study was done was to improve the treatment of future patients with cancer.	Agree*	Unsure*†	Disagree
There may not have been direct medical benefit to me/my child from participation.	Agree*	Unsure*†	Disagree
What of the following did you think was most likely to happen because of your participation in this research study?	I/My child would have a better chance of being cured.	Doing this testing would give me peace of mind.*	Doctors would be better able to find cures for future patients.*
	Doctors would be able to learn more about my/my child's cancer.*	I/my child would have a greater number of treatment options.*	Nothing was likely to happen as a result of this research.*
	I would learn about my/my child's genes.*	I would learn about my family's genes.*	Other*

*These answer choices were indications of participant understanding (Fig 1).
†Answer choices were excluded from sensitivity analyses (Appendix Fig A1 and Appendix Table A2).

alterations for which a matched targeted therapy was available via clinical trial or US Food and Drug Administration–approved medication; the recommendation described actionable alteration(s) found and strength of evidence for each treatment recommendation.

Study Population

iCat participants were offered a self-administered written survey after return of study results to the patient's oncologist. Surveys were offered in English to the consenting individual: the patient if he/she was age 18 years or older at enrollment, or the patient's parent/guardian if the patient was younger than age 18 years at enrollment. Surveys were not offered if the patient died between the time of enrollment and approach by the study team (n = 41); the patient/parent did not understand English sufficiently to complete the survey (n = 3); the patient/parent declined additional contact from study investigators after enrollment (n = 0); and/or the oncologist did not permit approach by the study team (n = 4).

Survey Methods

Survey procedures have been reported previously.[24] Surveys consisted of 103 items and included scales that addressed participant understanding of the purpose of clinical research,[34] genetic knowledge,[35] and the short form-36 general health perceptions question. The primary outcome of interest was participant understanding. Secondary outcomes were participant-level predictors of understanding (demographic characteristics, genetic knowledge, experience with genetics, clinical status, receipt of iCat recommendation/targeted therapy). Eligible participants were approached at least 4 weeks after the return of sequencing results. Participants were enrolled between September 2012 and November 2013; surveys were administered between September 2014 and July 2015.

Participant Understanding of the Purpose of Research Sequencing

We assessed participant understanding with four independent items (Table 1). Three items were adapted from the Quality of Informed Consent measure—a validated measure to assess understanding of the purpose of oncology clinical trials,[34] by adult patients with cancer and further validated in parents of children with cancer[1]; answer choices were agree, unsure, and disagree.[34] The fourth item offered respondents multiple choices about their perceived most likely result of study participation.

Participants were asked how well they understood conversation(s) they had with the doctor about the iCat study and the testing involved in it, and responses were collected on a 5-point Likert scale (responses of extremely well, well, moderately, poorly, extremely poorly). They were also asked to respond to the statement, "I feel I have helped myself/my child by participating in this study" (responses of extremely true, very true, somewhat true, a little true, not at all true).

Genetic Knowledge/Experience

Genetic knowledge was assessed with four items from the Genetic Knowledge Index (GKI) about the role of genetics in disease prevention/cure, genetic determinism, heredity, and the role of genetics in health (Appendix Table A1).[35] This validated scale previously has been used

to measure patient knowledge about genetics/genomics.[24,36,37] Respondents were asked if they had regular exposure to genetics and/or genetic information through their job and if they had ever attended any classes/lectures on genes/genetics.

Statistical Methods

Understanding of the purpose of the study was defined in two ways. Basic understanding was defined as accurate recognition that the primary purpose of participation was not to improve their/their child's treatment (Table 1). Comprehensive understanding was defined as an understanding of all four of the following: (1) the primary purpose was not to improve their/their child's treatment; (2) the primary purpose was to improve treatment of future patients with cancer; (3) there may not have been direct medical benefit to them/their child; and (4) the most likely result of participation was not an increased likelihood of cure for themselves/their child. Participants who correctly answered all four items were coded as having comprehensive understanding; those who answered zero to three items correctly did not. For example, if a participant identified that the primary purpose of the study was not to improve her child's treatment, he or she demonstrated basic understanding of the study's purpose. If he or she incorrectly answered any (or all) of the other three understanding items, he or she did not demonstrate comprehensive understanding. To be as inclusive as possible, and because of the complexity and uncertainty inherent in tumor profiling research, responses of unsure to any of the first three items were coded as consistent with understanding. Sensitivity analyses were performed to exclude responses of unsure from analysis. For the fourth item, only responses that the most likely result of participation in the study was cure were coded as inconsistent with understanding; all other responses, including answers of other, were coded as understanding. Missing responses to any of the four understanding items were excluded from analysis of comprehensive understanding; only those that were missing the first item were excluded from analysis of basic understanding.

Self-report of degree of understanding of the consent conversation(s) was dichotomized as well or extremely well (coded as good self-reported understanding) versus all others. Those who answered extremely true or very true to the item about how helpful participation was to them/their child were coded as feeling the study to have been helpful, and those who answered with the other answer choices were coded as feeling it was not.

Experience with genetics was defined as an affirmative response to questions of regular exposure to genetics or experience with genetics/genetic information and/or enrollment in any classes/lectures on genes or genetics. High genetic knowledge was defined as correct answers of all four items from the GKI.[35] Those who answered fewer than four GKI items correctly were coded as having low genetic knowledge.

Respondent demographics and clinical characteristics and understanding of results and the purpose of testing were evaluated using descriptive statistics. Bivariable associations between respondent characteristics and understanding of the purpose of tumor profiling were conducted using Fisher's exact test. Item nonresponse was less than 10%, and participants with nonresponse to an item were excluded from analyses of that item. All analyses were performed using Stata, version 13.1 (StataCorp, College Station, TX).

RESULTS

Respondent Characteristics

Of 101 participants who underwent profiling on the iCat study, 53 were eligible for survey administration. Forty-five surveys (85%) were completed. Surveys were completed a median of 13.5 months (interquartile range, 11.2 to 18.8 months) after the return of results to clinicians and 22.6 months (interquartile range, 19.1 to 24.0 months) after study enrollment. Characteristics of survey respondents are listed in Table 2 for the overall cohort and are subdivided into patient (n = 11; 24%) and parent/guardian (n = 34; 76%) respondents. Characteristics of patients themselves are also listed and subdivided similarly. Sixty-two percent of participants reported a good understanding of what they were told about the iCat study and its involved testing.

Participant Understanding

Nearly all survey participants (44 of 45, or 98%) correctly stated that, by participation in

Table 2. Participant and Patient Demographics, Overall and Separately, According to Whether the Survey Was Completed by the Patient's Parent/Guardian or by the Patient Himself or Herself

Variable	No. (%)		
	Overall (N = 45)	Parent/Guardian Respondents (n = 34)	Patient Respondents (n = 11)
Survey respondent characteristic			
Age, years			
≥ 40	26 (58)	26 (76)	0 (0)
< 40	19 (42)	8 (24)	11 (100)
Sex			
Male	18 (40)	10 (29)	8 (73)
Female	27 (60)	24 (71)	3 (27)
Education			
College graduate and higher	26 (58)	23 (68)	3 (27)
Less than college graduate	19 (42)	11 (32)	8 (73)
Race/ethnicity			
White, non-Hispanic	25 (56)	20 (59)	5 (45)
Non-white or Hispanic	20 (44)	14 (41)	6 (55)
Experience with genetics and/or genetic testing			
No	14 (31)	12 (35)	2 (18)
Yes	31 (69)	22 (65)	9 (82)
Genetic knowledge*			
Low genetic knowledge	13 (32)	8 (25)	5 (56)
High genetic knowledge	28 (68)	24 (75)	4 (44)
Patient characteristic			
Age, years			
< 2	3 (7)	3 (9)	0 (0)
2-9	15 (33)	15 (44)	0 (0)
10-17	16 (36)	16 (47)	0 (0)
≥ 18	11 (24)	0 (0)	11 (100)
Sex			
Male	26 (58)	18 (53)	8 (73)
Female	19 (42)	16 (47)	3 (27)
Diagnosis			
Ewing sarcoma	5 (11)	2 (6)	3 (27)
Neuroblastoma	6 (13)	5 (15)	1 (9)
Osteosarcoma	3 (7)	3 (9)	0 (0)
Renal tumors	6 (13)	5 (15)	1 (9)
Rhabdomyosarcoma	6 (13)	6 (18)	0 (0)
Other sarcoma	12 (27)	7 (21)	5 (45)
Other diagnosis	7 (16)	6 (18)	1 (9)
Site			
DFCI	30 (67)	25 (74)	5 (45)
Columbia	4 (9)	2 (6)	2 (18)
CNMC	5 (11)	3 (9)	2 (18)
UCSF	6 (13)	4 (12)	2 (18)

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Table 2. Participant and Patient Demographics, Overall and Separately, According to Whether the Survey Was Completed by the Patient's Parent/Guardian or by the Patient Himself or Herself (Continued)

Variable	No. (%)		
	Overall (N = 45)	Parent/Guardian Respondents (n = 34)	Patient Respondents (n = 11)
Participant-reported health status*			
Excellent/very good	26 (59)	22 (67)	4 (36)
Good/fair/poor	18 (41)	11 (33)	7 (64)
Participant-reported likelihood of cure			
≥ 60% chance	26 (58)	21 (62)	5 (45)
< 60% chance	19 (42)	13 (38)	6 (55)
Receiving treatment at time of survey completion			
No	24 (53)	17 (50)	7 (64)
Yes	21 (47)	17 (50)	4 (36)
Received iCat treatment recommendation			
No	33 (73)	24 (71)	9 (82)
Yes	12 (27)	10 (29)	2 (18)
Received targeted treatment			
No	44 (98)	33 (97)	11 (100)
Yes	1 (2)	1 (3)	0 (0)
Respondent attitude about iCat study			
Understanding of iCat information			
Poor self-reported understanding	17 (38)	12 (35)	5 (45)
Good self-reported understanding	28 (62)	22 (65)	6 (55)
Helpfulness of participating in this study			
Not helpful to myself/my child	25 (56)	18 (53)	7 (64)
Helpful	20 (44)	16 (47)	4 (36)

Abbreviations: DFCI, Dana-Farber Cancer Institute; CNMC, Children's National Medical Center; UCSF, University of California at San Francisco; iCat, individualized cancer therapy.

*Genetic knowledge was unknown for four participants, and health status was unknown for one participant.

the study, they were helping doctors and scientists learn information that may benefit future patients with cancer; 89% (39 of 44 respondents) also stated that they believed their participation was helping doctors and scientists learn information that may benefit them/their child.

Figure 1 depicts participant responses to survey items that addressed understanding of the purpose of participation in the iCat research study (data with responses of unsure excluded are shown in Appendix Fig A1). Sixty-eight percent of respondents (30 of 44 respondents) recognized that the primary reason the study was performed was not to improve the treatment of them/their child, which met our definition of basic understanding of the purpose of the study. Fifty-five percent (24 of 44 respondents) demonstrated comprehensive understanding according to the composite four-item definition, including 98% (43 of 44 respondents) who indicated that the primary reason for the study was to improve treatment of future patients with cancer, 93% (41 of 44 respondents) who recognized that there may not have been direct benefit to them/their child by participating, and 82% (37 of 45 respondents) who recognized that the most likely result of participation was not a better chance of being cured.

Basic understanding was seen more frequently among those who had at least a college education (81% *v* 50%; $P = .05$; Table 3), who had higher genetic knowledge (82% *v* 46%; $P = .03$), and who were not receiving cancer-directed therapy at the time of survey completion (83% *v* 52%;

P = .05). No significant differences were seen according to respondent age, sex, or race/ethnicity; according to self-reported health status or likelihood of cure, receipt of an iCat treatment recommendation or matched targeted therapy; or according to participant-identified understanding of what they were told about the study. Results were similar when responses of unsure were excluded from analysis (Appendix Fig A1).

Similar results were seen with understanding defined by the composite four-item scale. Comprehensive understanding of the purpose of genomic profiling research was seen with statistically greater frequency among those with at least a college education (73% *v* 28%; P = .01) and with higher genetic knowledge (71% *v* 23%; P = .01) and among white/non-Hispanic respondents (68% *v* 37%; P = .07), though the comparison by race/ethnicity was not statistically significant. Statistically significant differences in respondent understanding were not seen according to respondent age, sex, self-reported health status, or likelihood of cure. Similarly, no statistical difference in understanding was seen according to receipt of an iCat treatment recommendation or matched targeted therapy or according to whether the respondent reported a good understanding of what they were told about the study/testing. Decreased understanding was seen in those who stated that participation in the study had been helpful to them/their child (35% *v* 71%; P = .03). Sensitivity analyses that excluded responses of unsure provided similar findings (Appendix Table A2). Time between return of results and survey completion did not differ statistically between participants with and without basic understanding (median, 13.3 *v* 16.0 months; P = .31) or comprehensive understanding (median, 13.2 *v* 15.0 months; P = .34).

Many participants recognized dual roles for this study. Among those who mistakenly identified the primary purpose as improvement of their/their child's treatment, 93% (13 of 14 respondents) simultaneously recognized that it aimed to benefit future patients. Ninety-three percent (13 of 14 respondents) of this subgroup also correctly reported that they/their child might not have directly benefited from participation. All respondents who stated that the most likely result of participation was increased chance of cure also identified benefit for future patients as the study's primary purpose. Twenty-eight percent (12 of 43 respondents) of those who identified that the primary purpose was to benefit future patients also reported that the primary purpose was to improve their/their child's treatment.

DISCUSSION

In this multi-institutional study that examined the role of molecular profiling of pediatric solid tumors, nearly all participants recognized that the primary purpose was to benefit future patients. However, approximately one third of respondents believed that the primary purpose of the trial was to improve their/their child's treatment, and nearly one fifth expected participation to impart a greater chance of cure.

Although these responses raise concerns about the quality of informed consent for tumor

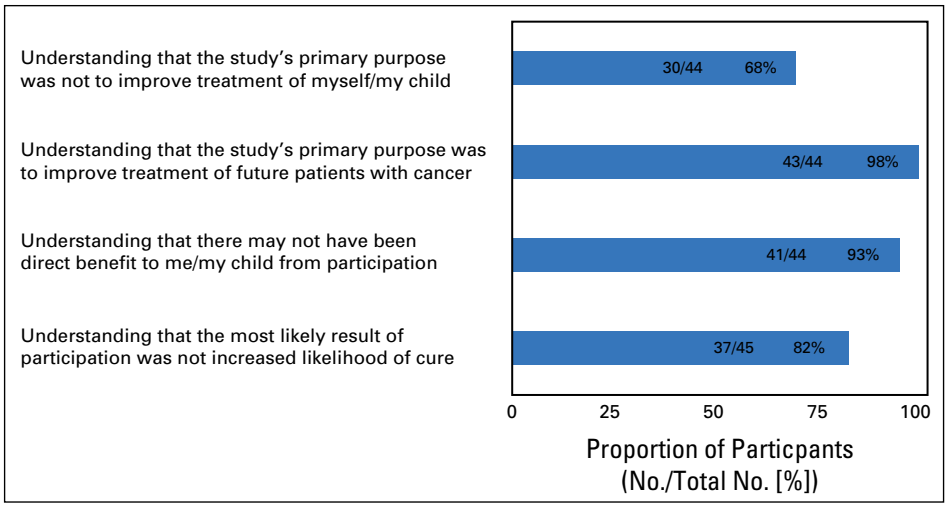

Fig 1. Participant understanding of the purpose of participation.

Table 3. Relationship Between Participant Demographics and Understanding of Purpose of Research Tumor Profiling

	Basic Understanding		Comprehensive Understanding	
	No. (%)	*P*	No. (%)	*P*
Survey respondent characteristic	30/44 (68)		24/44 (55)	
Age, years		.75		.22
≥ 40	18 (72)		16 (64)	
< 40	12 (63)		8 (42)	
Sex		.99		.36
Male	12 (67)		8 (44)	
Female	18 (69)		16 (62)	
Education		.05		.01
College graduate and higher	21 (81)		19 (73)	
Less than college graduate	9 (50)		5 (28)	
Race/ethnicity		.33		.07
White, non-Hispanic	19 (76)		17 (68)	
Non-white or Hispanic	11 (58)		7 (37)	
Experience with genetics and/or genetic testing		.32		.34
No	8 (57)		6 (43)	
Yes	22 (73)		18 (60)	
Genetic knowledge*		.03		.01
Low genetic knowledge	6 (46)		3 (23)	
High genetic knowledge	23 (82)		20 (71)	
Survey completer		.29		.08
Parent/guardian	24 (73)		21 (64)	
Patient	6 (55)		3 (27)	
Patient characteristic				
Participant-reported health status*		.99		.99
Excellent/very good	17 (65)		14 (54)	
Good/fair/poor	12 (71)		9 (53)	
Participant-reported likelihood of cure		.21		.37
≥ 60% chance	15 (60)		12 (48)	
< 60% chance	15 (79)		12 (63)	
Receiving treatment at time of survey completion		.05		.23
No	19 (83)		15 (65)	
Yes	11 (52)		9 (43)	
Received iCat treatment recommendation		.72		.33
No	21 (66)		19 (59)	
Yes	9 (75)		5 (42)	
Received targeted treatment		.99		.99
No	29 (67)		23 (53)	
Yes	1 (100)		1 (100)	
Respondent attitude about iCat study				
Understanding of iCat information		.18		.12
Poor self-reported understanding	14 (82)		12 (71)	
Good self-reported understanding	16 (59)		12 (44)	

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Table 3. Relationship Between Participant Demographics and Understanding of Purpose of Research Tumor Profiling (Continued)

	Basic Understanding		Comprehensive Understanding	
	No. (%)	*P*	No. (%)	*P*
Helpfulness of participating in the study		.11		.03
Not helpful to myself/my child	19 (79)		17 (71)	
Helpful	11 (55)		7 (35)	

NOTE. Values within the table represent frequencies (row percentages).

Abbreviation: iCat, individualized cancer therapy.

*Genetic knowledge was unknown for three participants, and health status was unknown for one participant.

sequencing, they must be considered in context of a complex technology with an evolving role in clinical care. Importantly, participants often felt that sequencing had dual roles, with potential benefits not only to future patients but also to themselves/their children. This duality is echoed by the American Society of Clinical Oncology, which states that early-phase clinical trials in oncology simultaneously generate new knowledge and provide participants the opportunity for psychological and clinical benefit.[22,38] Oncologists often balance dual goals for patients by recommending enrollment in a phase I trial while hoping for patient benefit or by simultaneously providing palliative and cancer-directed (ie, blended) care.[39] In the era of precision cancer medicine, it is reasonable that patients/families might perceive such dualities as well.

This duality has important clinical implications. If patients/parents frequently identify dual goals when they participate in sequencing research, consenting clinicians should query and explore these goals during presequencing counseling. Additional work is needed to better understand how participants conceptualize and balance dual goals in genomics research. However, an initial approach could be to discuss the primary goal of the study as gaining new knowledge to help future patients, followed by an acknowledgment, tempered with realistic expectations, that many patients/parents—and many clinicians—hold hope that the child will also benefit from participation. In the case of next-generation sequencing, for example, it is important to note that the number of patients who experience direct benefit via receipt of a targeted therapy is quite low, likely in the range of 3% to 19%.[25-29]

Our results also underscore the importance of hope among patients and parents of children with cancer in clinical and research settings.[40-42] Hopeful thinking may partially explain why participants who felt the study had helped them/their child and those who were receiving cancer-directed therapy at the time of survey completion less frequently demonstrated understanding of the purpose of research tumor sequencing.

In this cohort, understanding was observed more frequently in those with at least a college education and those with good genetic knowledge. This finding, also reported elsewhere,[23] is not surprising, given the complexity of these concepts and the expected link between understanding and health literacy/numeracy.[43] Understanding also varied according to race/ethnicity, consistent with similar work in the pediatric oncology phase I literature,[2] although the difference did not reach statistical significance in this pilot study. These disparities underscore the importance of attention to the needs of vulnerable populations when they are counseled about genomic results; however, the optimal mechanism for such counseling remains unclear.[44]

Prior work in pediatric oncology has identified that refinement of the consent process may improve understanding,[45] but optimal strategies to adequately convey the complexities of tumor sequencing and support fully informed consent for participation in sequencing research are not yet known. A follow-up study is in development to examine the benefit of such an intervention for those who demonstrate less than comprehensive understanding, as defined in this cohort. Tools such as these will become only more important as genomic sequencing becomes more frequently used in the clinical setting and as research explores the role of RNA sequencing, methylation profiling, or the next promising precision modality.

Data collected in this study are limited primarily by the cross-sectional nature and timing of survey administration. Patients/parents may have better understood the purpose of profiling closer to the time of consent, but understanding did not vary statistically with time to survey completion in this cohort. Some may also disagree with how understanding was defined in this work. Individual respondents may have felt that the primary purpose of the study for them was different than it was for the researchers, for example. These definitions were considered a starting point to clarify the complex issues inherent in studies of pediatric tumor profiling. The use of validated items to define understanding[1,34] and the similar results for both basic and comprehensive understanding support these definitions. Also, variability in consent discussions could have affected participant understanding of the study's purpose. Additional work is necessary to isolate the role of these important considerations.

Respondents were queried after return of sequencing results, which could have affected their responses. Many study participants died before surveys could be administered; however, demographic and clinical characteristics of respondents mirrored those of the overall cohort.[25] Finally, participants were enrolled at four large academic centers, so results may not be generalizable to those from smaller and/or community centers. This could, for example, explain the unexpectedly high genetic knowledge and experience seen in this cohort.

Although some participants misidentified the primary goal of tumor profiling research as therapeutic in nature, participant views are nuanced. Nonetheless, some populations demonstrate decreased understanding of the purpose of tumor profiling research and warrant special attention to ensure equitably informed consent for all research participants. Interventional work to improve participant understanding of these complexities and nuances is necessary as sequencing moves from the laboratory to the clinic. Such work can guide pediatric oncologists in how to manage expectations and best counsel patients and families about the meaning and significance of clinical profiling results.

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AUTHOR CONTRIBUTIONS:

Conception and design: Jonathan M. Marron, Katherine A. Janeway, Jennifer W. Mack

Collection and assembly of data: Jonathan M. Marron, Steven G. DuBois, Julia Glade-Bender, AeRang Kim, Brian D. Crompton, Stephanie C. Meyer

Provision of study material or patients: Steven G. DuBois, Julia Glade-Bender, AeRang Kim, Katherine A. Janeway

Data analysis and interpretation: Jonathan M. Marron, Angel M. Cronin, Julia Glade-Bender, AeRang Kim, Jennifer W. Mack

Administrative support: Jonathan M. Marron

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Manuscript writing: All authors

Final approval of manuscript: All authors

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Jonathan M. Marron
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Angel M. Cronin
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Steven G. DuBois
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AeRang Kim
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Brian D. Crompton
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Affiliations

Jonathan M. Marron, **Angel M. Cronin**, **Steven G. DuBois**, **Brian D. Crompton**, **Stephanie C. Meyer**, **Katherine A. Janeway**, and **Jennifer W. Mack**, Dana-Farber Cancer Institute; **Jonathan M. Marron**, **Steven G. DuBois**, **Brian D. Crompton**, **Stephanie C. Meyer**, **Katherine A. Janeway**, and **Jennifer W. Mack**, Dana-Farber/Boston Children's Cancer and Blood Disorders Center; **Jonathan M. Marron**, **Steven G. DuBois**, **Brian D. Crompton**, **Katherine A. Janeway**, and **Jennifer W. Mack**, Harvard Medical School; **Jonathan M. Marron**, Boston Children's Hospital, Boston, MA; **Julia Glade-Bender,** Columbia University Medical Center, New York, NY; and **AeRang Kim**, Children's National Medical Center, Washington, DC.

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Appendix

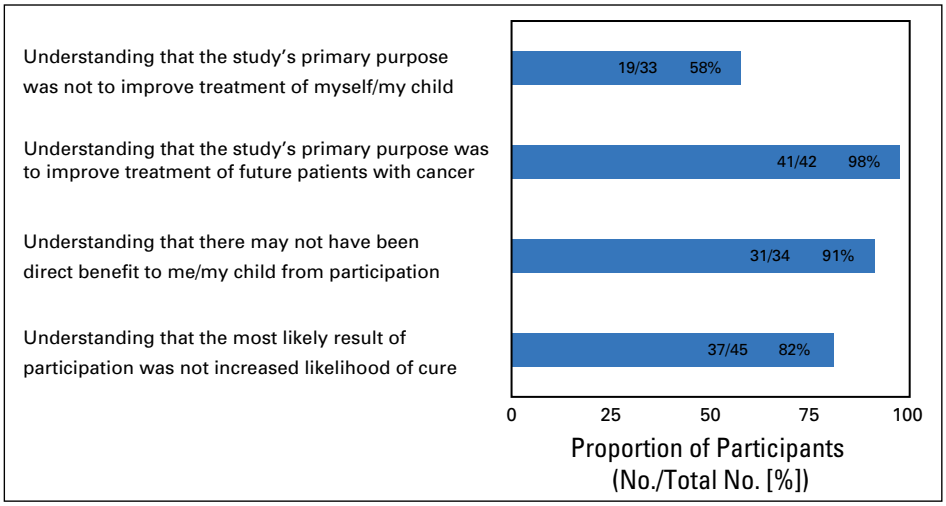

Fig A1. Participant understanding of the purpose of participation (responses of unsure were excluded).

Table A1. Survey Items for Assessment of Participant Genetic Knowledge

Question Stem	Answer Choice	
Once a genetic marker for a disorder is identified in a person, the disorder can be prevented or cured.	True	False*
If a person has a genetic marker for a disorder, the person will always get the disorder.	True	False*
Only mothers can pass on genetic disorders.	True	False*
People who have a genetic marker for a disease are unhealthy.	True	False*

NOTE. All items adapted from the Genetic Knowledge Index.[35]
*Correct answer.

Table A2. Sensitivity Analyses for the Relationship Between Participant Demographics and Understanding of the Purpose of Research Tumor Profiling

	Basic Understanding (n = 33)		Comprehensive Understanding (n = 26)	
Variable	**No. (%)**	***P***	**No. (%)**	***P***
Survey respondent characteristic	19 (58)		16 (62)	
Age, years		.27		.99
≥ 40	14 (67)		12 (63)	
< 40	5 (42)		4 (57)	
Sex		.72		.66
Male	6 (50)		4 (50)	
Female	13 (62)		12 (67)	
Education		.03		.19
College graduate and higher	15 (75)		13 (72)	
Less than college graduate	4 (31)		3 (38)	
Race/ethnicity		.30		.42
White, non-Hispanic	12 (67)		11 (69)	
Non-white or Hispanic	7 (47)		5 (50)	
Experience with genetics and/or genetic testing		.46		.37
No	5 (45)		3 (43)	
Yes	14 (64)		13 (68)	
Genetic knowledge*		.02		.16
Low genetic knowledge	3 (30)		2 (33)	
High genetic knowledge	16 (76)		14 (70)	
Survey completer		.11		.99
Parent/guardian	17 (65)		14 (61)	
Patient	2 (29)		2 (67)	
Patient characteristic				
Participant-reported health status		1.00		.42
Excellent/very good	11 (55)		10 (56)	
Good/fair/poor	8 (62)		6 (75)	
Participant-reported likelihood of cure		.16		.25
≥ 60% chance	8 (44)		7 (50)	
< 60% chance	11 (73)		9 (75)	
Receiving treatment at time of survey completion		.29		.23
No	10 (71)		10 (77)	
Yes	9 (47)		6 (46)	
Received iCat treatment recommendation		.99		.64
No	15 (58)		13 (65)	
Yes	4 (57)		3 (50)	
Received targeted treatment		.99		.99
No	18 (56)		15 (60)	
Yes	1 (100)		1 (100)	

(Continued on following page)

Table A2. Sensitivity Analyses for the Relationship Between Participant Demographics and Understanding of the Purpose of Research Tumor Profiling (Continued)

	Basic Understanding (n = 33)		Comprehensive Understanding (n = 26)	
Variable	**No. (%)**	***P***	**No. (%)**	***P***
Respondent attitudes about iCat study				
Understanding of iCat information		.09		.22
Poor self-reported understanding	10 (77)		8 (80)	
Good self-reported understanding	9 (45)		8 (50)	
Helpfulness of participating in iCat study		.30		.23
Not helpful to myself/my child	11 (69)		10 (77)	
Helpful	8 (47)		6 (46)	

NOTE. Responses of unsure were excluded. Values within the table represent frequencies (row percentages).

Abbreviation: iCat, individualized cancer therapy.

*For the analysis of basic understanding, genetic knowledge was unknown for two participants.