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Patient/parent perspectives on genomic tumor profiling of pediatric solid tumors: The Individualized Cancer Therapy (iCat) experience

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Abstract

Background—Genomic tumor profiling (GTP) plays an important role in the care of many adult cancer patients. Its role in pediatric oncology is still evolving, with only a subset of patients currently expected to receive clinically significant results. Little is known about perspectives of pediatric oncology patients/parents on GTP.

Procedure—We surveyed individuals who previously underwent GTP through the iCat (Individualized Cancer Therapy) pilot study of molecular profiling in children with relapsed, refractory, and high-risk solid tumors at four pediatric cancer centers. Following return of profiling results, a cross-sectional survey was offered to the patient, if ≥18y at enrollment, or parent, if <18y. Forty-five surveys (85% response) were completed.

Results—Eighty-nine percent (39/44) of respondents reported hoping participation would help find cures for future patients, while 59% (26/44) hoped it would increase their/their child's chance of cure. Most had few concerns about GTP, but 12% (5/43) worried they would learn their/their child's cancer was less treatable or more aggressive than previously thought. Sixty-four percent (29/45) reported feeling their participation had helped others, and 44% (20/45) felt they had helped themselves/their own child, despite only one sub-study subject receiving targeted therapy

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CONFLICT OF INTEREST STATEMENT

None of the authors have any relevant conflicts of interest to report.

matched to GTP findings. Fifty-four percent (21/39) wished to receive all available profiling data, including findings unrelated to cancer and of unclear significance.

Conclusions—Participants in pediatric GTP research perceive benefits of GTP to themselves and others, but expectations of personal benefits of GTP may exceed actual positive impact. These issues warrant consideration during consent discussions about GTP research participation.

Keywords

personalized medicine; pediatric oncology; cancer; molecular profiling; genomics; patient perspectives

INTRODUCTION

Survival outcomes in pediatric oncology are better today than at any point in history,[1] but some diagnoses continue to portend dismal prognoses. Many relapsed, recurrent, and high-risk pediatric solid tumors carry mortality rates of 75% or higher.[2–6] Precision cancer medicine is one strategy currently being studied in attempt to improve outcomes for this patient population. In the care of adult cancer patients, genomic tumor profiling (GTP) is rapidly becoming the standard of care for some cancer subtypes, and a growing appreciation of the genomic underpinnings of cancer has led to the development of targeted therapies such as imatinib,[7,8] vemurafenib,[9,10] crizotinib,[11,12] and trastuzumab.[13,14] In parallel, clinical trials focusing on particular molecular alterations rather than cancer diagnoses represent a paradigmatic shift in clinical trial design.[10,15,16] In the care of pediatric cancer patients, molecular profiling shows similar promise,[17–20] and early-phase clinical trials assessing the feasibility of molecular profiling and the utilization of targeted therapies in pediatric cancer suggest a growing role for both in pediatric oncology.[21–24] Despite this promise, the role and utility of GTP in the care of pediatric cancer patients require further study prior to gaining acceptance as a standard element of clinical care.

Little is known about patients' and parents' hopes, goals, and expectations for GTP in pediatric oncology. Recent research suggests that adult patients attach significant and perhaps unrealistic hopes to somatic genomic testing: over 30% of adults have misperceptions about the utility of somatic genomic testing,[25,26] and 64% of adults with advanced cancer believe that such profiling would significantly improve their cancer care.[27] Additionally, fewer than half of patients believe they have sufficient knowledge to make an informed decision of whether to pursue somatic profiling of their tumor.[27] Though efforts have begun to explore how to improve the quality of informed consent in pediatric cancer genomics research,[28,29] limited data are available on the pediatric oncology population's hopes and concerns about molecular profiling, what they expect of the testing, and how it impacts them.

Complicating matters further, no consensus exists regarding the return of profiling results to patients and families. In 2013, the American College of Medical Genetics and Genomics (ACMG) published recommendations regarding the return of incidental germline findings from next-generation sequencing,[30] but these guidelines remain controversial and were later amended following significant public debate.[31,32] Recent work has identified that

many more children with cancer may have cancer predisposition syndromes than previously thought,[33] but little is known about families' preferences for learning such germline information. Investigators have explored parents' preferences for return of results in pediatric genomic sequencing research,[34] but no data are presently available regarding which results pediatric oncology patients and families wish to receive following this type of testing.

A recent qualitative analysis of parents of children with cancer who underwent somatic and germline whole exome sequencing reported that parents do not expect such testing to be "ethically disruptive" but rather see it as an important new component of the care of their children.[35] With the study described here, we aimed to build upon these important findings and describe in a quantitative fashion the perspectives of enrollees on a clinical trial of molecular profiling of pediatric solid tumors following return of sequencing results. Specifically, we looked to analyze patients' and parents' hopes, expectations, and concerns about GTP, its impact on participants and their families, and participants' preferences regarding the return of profiling results.

METHODS

We conducted a cross-sectional questionnaire-based study of participants in the multi-institutional iCat (**I**ndividualized **Ca**ncer **T**herapy) pilot study of molecular profiling in children with relapsed, recurrent, and high-risk solid tumors (NCT01853345).[23] Participants were enrolled at four tertiary pediatric cancer centers: the Dana-Farber/Boston Children's Cancer and Blood Disorders Center (Boston, MA), the University of California at San Francisco (San Francisco, CA), Columbia University Medical Center (New York, NY), and Children's National Medical Center (Washington, DC). This study was approved by the Institutional Review Board of each participating institution. Surveys were administered between September 2014 and July 2015.

The iCat study

A detailed description of the methodology utilized in the iCat molecular profiling study can be found elsewhere.[23] Briefly, subjects were eligible for enrollment if they were ≤30 years at enrollment and had a recurrent, refractory, or high-risk extracranial solid tumor with sufficient tumor specimen available for submission. All subjects and/or their parent/guardian provided informed consent/assent, with all offered the opportunity to opt out of having GTP results reported back to their oncologist. Following tumor profiling via a Sequenom assay or targeted next-generation sequencing and copy number assessment, a multi-disciplinary expert panel reviewed all available profiling results. This panel reviewed available literature to identify clinically significant results from each tumor sample and sent a letter to the treating oncologist alerting them to the presence or absence of such results, along with any variants that might suggest a change in diagnosis or possible cancer predisposition syndrome. For subjects with relapsed or recurrent disease, if actionable alterations (defined as those that could potentially be targeted by a matched therapy) were found and a matched targeted therapy was available via a clinical trial or FDA-approved medication, the panel

included in the letter an “iCat recommendation” describing the actionable alteration(s) found and the strength of the available evidence for the recommendation.

Study population

Participants in the iCat study were offered a self-administered written survey following return of iCat results to each subject’s oncologist. English-language surveys were offered to the individual who consented to profiling: the patient him/herself if he/she was ≥18 years at the time of study enrollment, or his/her parent, if the patient was <18 years at enrollment. All iCat enrollees were offered enrollment in this sub-study, save those who met the following exclusion criteria: a) the patient died between the time of initial enrollment on the iCat study and that of approach by the study team (N=41); b) the patient/parent did not understand English sufficiently to complete the questionnaire (N=3); or c) the treating oncologist did not provide permission for the study team to approach the patient/parent (N=4). Of 101 subjects for whom molecular profiling was attempted on the iCat study, 53 were eligible for this sub-study, and 45 surveys (85%) were completed.

Data collection

The survey instrument utilized validated measures when available, including the Quality of Informed Consent measure,[36] Genetic Knowledge Index,[37] and the SF-36 general health perceptions question (SF-1). Measures were adapted as necessary to ensure their applicability to this study population. Remaining items were novel, based on available literature and expert opinion.[25–27,38–41] All items were vetted with experts in survey methodology, pediatric oncology, cancer genomics, and bioethics and were pilot tested via ten face-to-face interviews with pediatric solid tumor patients/parents. Survey instruments for young adult patients and parents were identical, save for replacement of the word “you” with “your child.” The intent was to approach eligible respondents no sooner than one month following report of sequencing results to the treating oncologist via the iCat letter to allow adequate time for discussion of results. Additional data regarding patient diagnosis, iCat enrollment date, and receipt of iCat treatment recommendation and matched targeted therapy were procured from iCat data collection forms.

Survey domains and operational definition of variables

The 103-item instrument addressed domains including respondent hopes, expectations, and concerns about participation in GTP research, results of participation, and preferences for return of sequencing data. Participants were asked separately about what they hoped would happen as a result of the testing and what they felt was most likely to happen, in attempt to parse these two distinct but related constructs. Items addressing hopes/expectations/concerns about testing and results of participation were queried using 5-point Likert items (scaled from “extremely true” to “not true at all”). Responses of “extremely true” or “very true” were coded as positive, with the remainder as negative. Remaining items were multiple-choice, true/false, or yes/no. The survey instrument administered to young adult patients can be found online (Supplemental File S1).

Statistical analysis

Respondent characteristics, hopes and concerns about profiling, understanding of profiling, results of participation, and preferences for return of results were described with frequencies. McNemar's exact test was applied for comparison of respondent hopes/concerns about participation with actual results of participation. Sensitivity analyses were performed according to median time from return of sequencing results to survey completion and according to respondent type (young adult patient versus parent/guardian)., All analyses were performed using the SAS v9.4 statistical package (SAS Institute, Inc, Cary, NC).

RESULTS

Surveys were completed 4.2–29.1 months following return of results (median 13.5 months, interquartile range 11.2–18.8) and 10.0–38.3 months following study enrollment (median 22.6, interquartile range 19.1–24.0). Eleven surveys (24%) were completed by young adult (18–30y) patients, with the remainder by the minor child's parent/guardian (TABLE 1). Fifty-six percent of participants were white, and 58% had at least a college degree. Most (69%, 31/45) reported prior experience with genetics/genetic testing: prior coursework in genetics (51%); prior genetic testing (27%); and/or regular exposure to or experience with genetics through their occupation or other means (13%). Twelve (27%) survey respondents received an iCat recommendation. Of those, only one (2% of all survey respondents) received a targeted therapy matched to this recommendation during the study period. Though iCat sequencing was only offered to those with relapsed, recurrent, or high-risk (defined as overall survival estimated to be ≤25%) disease, 33% of survey respondents reported that at the time of survey completion that they/their child had >80% likelihood of cure.

In sensitivity analyses, no significant differences were seen between the responses of early and late respondents or according to respondent type (young adult patient versus parent/guardian), but the size of this cohort may have precluded detection of small differences.

Hopes and expectations related to participation in GTP research

When asked to recall their hopes prior to testing, most respondents (96%, 42/44) reported having hoped their participation would help doctors and scientists learn more about the genes involved in cancer, and 89% (39/44) had hoped it would help find cures for future patients. A majority also had hoped for direct benefit: 82% (26/44) had hoped their participation would provide information about their/their child's cancer, 72% (31/43) had hoped it would give them/their child more treatment options, and 59% (26/44) had hoped participating would increase their/their child's chance of cure.

When asked which benefit of testing they had expected to be most likely to happen, the most common response was that doctors would learn more about their/their child's cancer (31%, 14/45), followed by an increased chance of cure for future patients (24%, 11/45), and an increased chance of cure for themselves/their child (18%, 8/45). Only 4% (2/45) reported that they had not expected that any benefits were likely to result from this research.

Concerns related to participation in GTP research

Most recalled few concerns when queried about their perceptions at the time of enrollment, with 37% (16/43) reporting having had no concerns about participating in this research. The most frequently reported concern was that results would take a long time to come back (26%, 11/43). Twelve percent (5/43) of respondents stated they had worried they would learn that their/their child's cancer was less treatable or more aggressive than previously thought, and 16% (7/43) had worried that no new information would be found. Few reported concerns about loss of privacy (7%, 3/43), or that their participation would result in difficulty getting or keeping employment (2%, 1/43) or insurance (7%, 3/43).

When asked to recall which negative outcome they had expected was most likely to occur, 23% (10/43) stated they had expected no new information to be found, causing their family to be disappointed. Only two respondents (5%) stated the outcome they felt most likely to happen was that they would learn their/their child's cancer was less treatable or more aggressive than previously thought. Thirty-three percent (14/43) had not expected any negative impact from their participation.

Results of participation in GTP research

In response to survey items querying the impact of study participation on themselves/their child, 44% (20/45) stated that by participating, they had helped themselves/their child, and 64% (29/45) stated that doing so had helped others. No respondents stated that they regretted participating, that they/their child had been hurt by participating, that participating had caused them added stress/anxiety, or that participating had given them false hope (0/45 for each). Similarly, there were no reports of participation hurting a family's ability to get or keep employment or insurance.

The most commonly reported result of GTP research participation was increased hope for the identification of cures for future children with cancer (Table 2). However, more respondents reported having hoped for such an outcome at enrollment than reported actually having more hope for future cures after participating in the study (89% versus 56%, $p<0.001$). Twenty-seven percent of respondents stated that participating had given them hope that they/their child would be cured, while 59% stated that at study enrollment they had hoped that participating would give them such hope for themselves/their child ($p<0.001$). More respondents reported having hoped to receive new information about their/their child's cancer than reported actually receiving it (82% versus 24%, $p<0.001$), with the same true of new information about their/their child's genes (43% versus 14%, $p=0.008$). Similarly, a greater percentage had hoped that participating would provide them/their child with a greater number of treatment options than received an iCat recommendation that might provide such new possible treatments (72% versus 27%, $p<0.001$). No difference was seen between the number of participants who reported concern that they would be disappointed with results and the number who reported feeling such disappointment (16% versus 12%, $p=0.7$).

Preferences for return of GTP results and future genomics trial participation

As seen in Table 3, nearly all respondents wished to receive sequencing information that directed clinicians toward new treatment options (98%, 42/43) or that revealed that they/their

child were more likely to be cured than previously thought (93%, 39/42). A majority also wished to receive data about cancer mutations that did not suggest a new treatment option (81%), about cancer predisposition syndromes (86%), and about other heritable conditions (88%), with slightly fewer wishing to receive information about conditions that could not be prevented, screened, or treated (73%) or about variants of uncertain significance (78%). Just over half (56%) wished to be informed if results told clinicians that their/their child's cancer was less likely to be cured than previously thought. Fifty-four percent of respondents (21/39) wished to receive all queried subcategories of sequencing results. No differences were seen between the preferences of patients and parents/guardians.

Ninety-five percent (42/44) stated that they would enroll in another GTP research study if given the opportunity. Forty-eight percent (21/44) stated they would enroll even if enrollment required a tumor biopsy that they/their child would not otherwise need, with that number increasing to 77% (33/43) if their physician recommended the biopsy.

DISCUSSION

This study provides an important step toward understanding the perspectives of pediatric oncology patients and parents who have undergone tumor profiling. It demonstrates that this population is quite motivated to participate in cancer genomics research, as previously reported in other patient populations.[26,27,35,38] Furthermore, pediatric oncology patients and parents carry significant hopes for this technology, both for themselves/their children and for future children with cancer. In this cohort, these hopes exceeded the actual results experienced following receipt of sequencing data, particularly those regarding increased hope for cure. Participants in this study had fewer concerns related to this type of testing than previously reported in other studies of molecular profiling,[25,27] and they perceived little to no harm from their participation. These results must be considered in light of the fact that results were collected after sequencing results were returned, lending the possibility of recall bias, particularly given the variability in time from enrollment to survey completion.

The hope attached to genomic testing is understandable in this population of children with poor prognoses and their parents. This optimism mirrors the finding that iCat respondents reported a much higher likelihood of cure than would be expected based on their/their children's diagnoses. Such optimistic perspectives have been previously identified in parents of children with cancer.[42,43] We do not have data regarding the consent discussions between oncologists and patients/parents, but given prior reports of providers' perceptions of GTP,[26,44] it is possible that consenting oncologists in this study also held optimistic viewpoints about GTP. Further work is needed to understand the impact of the consenting provider on patient/parent perspectives on tumor profiling. It is not surprising that patients and parents hope participation in GTP research will improve their/their child's clinical outcome, but it is important that providers not excessively reinforce these hopes or transform them into expectations.

This study is limited primarily by the cross-sectional nature of the questionnaire and the length of time between study enrollment and survey completion. Additionally, we queried participants about their hopes/concerns once results had already been returned, which may

have led to biased reporting of these hopes/concerns. Given the limited number of positive clinical responses in this cohort, however, we would expect this bias to underestimate the difference between hopes/concerns and actual impact (toward the null).[45] Between-subject variability in time from reporting of sequencing results to survey completion may also have imparted some degree of recall bias, though this was not evident in our sensitivity analysis. Furthermore, though there was a wide range in survey response time, a majority of responses clustered around the median response time. Additionally, many patients who underwent GTP died before they/their parent could be surveyed; it is possible that perspectives of the full iCat population may have differed from those reported here. Finally, this cohort's size precludes a detailed analysis of factors associated with measured outcomes, and given that subjects were enrolled only at tertiary pediatric centers, reported perspectives may not fully reflect those of the population at-large.

Notably, we found significant interest in receiving nearly all available results from tumor sequencing, even results with no or unclear clinical significance, as has been reported elsewhere.[27,34,38] Only 54% of respondents wished to receive all types of results, however, when queried about each type individually. This finding, nearly identical to that seen in a recent study of parents' preferences for the return of genomic testing results about their children,[34] highlights the importance of comprehensive consent discussions with families prior to tumor profiling and suggests that it may be most appropriate to give enrollees the opportunity to opt out of receiving certain types of results. This would be in contrast to recent ACMG recommendations in support of reporting back particular incidental findings from clinical sequencing, regardless of the indication for sequencing.[30] The practical implementation of this, however, may be challenging, as the clinical significance of results can change with time. For example, at the time of sequencing, a mutation could be a variant of uncertain significance or even indicate a worse prognosis for the patient, but as research progresses, this same mutation could direct providers toward a newly-developed matched targeted therapy. This again speaks to the importance of detailed discussions prior to sequencing and availability of genetic counseling once results are returned.

Recent work has shown that informed consent discussions about sequencing can effectively increase patient knowledge about the benefits and limitations of sequencing,[46] indicating that a greater focus on informed consent may be an effective means of ensuring that participants have appropriate expectations upon enrollment into clinical genomics trials. As genomic tumor profiling moves from the realm of research to that of a clinical test, further studies looking at the utility of such consent discussions and interventional tools such as decision aids will be of great importance in determining the best means by which to educate patients/parents about this evolving technology.

Though only a limited number of molecularly targeted therapies presently are available for the care of children with cancer, participants in pediatric genomic profiling research have high hopes and expectations for this new technology, and many report significant benefits to themselves and their family with few associated concerns or harms. As part of the next phase of this work, we aim to further elucidate how these perspectives vary over time and with changes in clinical status via longitudinal data collection. As molecular profiling technologies continue to improve and more targeted therapies become available for pediatric

patients, the importance of comprehensive consent discussions with patients and families prior to enrollment in cancer genomics research will become only more significant, given the nuanced complexity of this research and the important distinction between hopes and expectations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

GTP	Genomic tumor profiling
iCat	Individualized Cancer Therapy
ACMG	American College of Medical Genetics and Genomics

References

1. Smith MA, Altekruse SF, Adamson PC, et al. Declining childhood and adolescent cancer mortality. Cancer. 2014; 120(16):2497–2506. [PubMed: 24853691]
2. Ferrari S, Luksch R, Hall KS, et al. Post-relapse survival in patients with ewing sarcoma. Pediatr Blood Cancer. 2015; 62(6):994–999. [PubMed: 25585917]
3. Leary SE, Wozniak AW, Billups CA, et al. Survival of pediatric patients after relapsed osteosarcoma: The st. Jude children's research hospital experience. Cancer. 2013; 119(14):2645–2653. [PubMed: 23625626]
4. Oberlin O, Rey A, Lyden E, et al. Prognostic factors in metastatic rhabdomyosarcomas: Results of a pooled analysis from united states and european cooperative groups. J Clin Oncol. 2008; 26(14): 2384–2389. [PubMed: 18467730]
5. Yu AL, Gilman AL, Ozkaynak MF, et al. Anti-gd2 antibody with gm-csf, interleukin-2, and isotretinoin for neuroblastoma. N Engl J Med. 2010; 363(14):1324–1334. [PubMed: 20879881]
6. Lager JJ, Lyden ER, et al. Soft Tissue Sarcoma Committee of the Children's Oncology G. Pooled analysis of phase ii window studies in children with contemporary high-risk metastatic rhabdomyosarcoma: A report from the soft tissue sarcoma committee of the children's oncology group. J Clin Oncol. 2006; 24(21):3415–3422. [PubMed: 16849756]
7. Druker BJ, Sawyers CL, Kantarjian H, et al. Activity of a specific inhibitor of the bcr-abl tyrosine kinase in the blast crisis of chronic myeloid leukemia and acute lymphoblastic leukemia with the philadelphia chromosome. N Engl J Med. 2001; 344(14):1038–1042. [PubMed: 11287973]
8. Kantarjian HM, Shah NP, Cortes JE, et al. Dasatinib or imatinib in newly diagnosed chronic-phase chronic myeloid leukemia: 2-year follow-up from a randomized phase 3 trial (dasision). Blood. 2012; 119(5):1123–1129. [PubMed: 22160483]
9. Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with braf v600e mutation. N Engl J Med. 2011; 364(26):2507–2516. [PubMed: 21639808]

10. Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in multiple nonmelanoma cancers with braf v600 mutations. N Engl J Med. 2015; 373(8):726–736. [PubMed: 26287849]
11. Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med. 2010; 363(18):1693–1703. [PubMed: 20979469]
12. Solomon BJ, Mok T, Kim DW, et al. First-line crizotinib versus chemotherapy in alk-positive lung cancer. N Engl J Med. 2014; 371(23):2167–2177. [PubMed: 25470694]
13. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against her2 for metastatic breast cancer that overexpresses her2. N Engl J Med. 2001; 344(11): 783–792. [PubMed: 11248153]
14. Perez EA, Romond EH, Suman VJ, et al. Four-year follow-up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: Joint analysis of data from ncctg n9831 and nsabp b-31. J Clin Oncol. 2011; 29(25):3366–3373. [PubMed: 21768458]
15. Redig AJ, Janne PA. Basket trials and the evolution of clinical trial design in an era of genomic medicine. J Clin Oncol. 2015; 33(9):975–977. [PubMed: 25667288]
16. McNeil C. NCI-MATCH launch highlights new trial design in precision-medicine era. J Natl Cancer Inst. 2015; 107:7.
17. Janeway KA, Place AE, Kieran MW, et al. Future of clinical genomics in pediatric oncology. J Clin Oncol. 2013; 31(15):1893–1903. [PubMed: 23589558]
18. Glade Bender J, Verma A, Schiffman JD. Translating genomic discoveries to the clinic in pediatric oncology. Curr Opin Pediatr. 2015; 27(1):34–43. [PubMed: 25502895]
19. Adamson PC. Improving the outcome for children with cancer: Development of targeted new agents. CA Cancer J Clin. 2015; 65(3):212–220. [PubMed: 25754421]
20. Schnepp RW, Bosse KR, Maris JM. Improving patient outcomes with cancer genomics: Unique opportunities and challenges in pediatric oncology. JAMA. 2015; 314(9):881–883. [PubMed: 26325556]
21. Mody RJ, Wu YM, Lonigro RJ, et al. Integrative clinical sequencing in the management of refractory or relapsed cancer in youth. JAMA. 2015; 314(9):913–925. [PubMed: 26325560]
22. Parsons D, Roy A, Yang Y, et al. Diagnostic yield of clinical tumor and germline whole-exome sequencing for children with solid tumors. JAMA Oncology. 2016; 2(5):616–624.
23. Harris MH, DuBois SG, Glade Bender JL, et al. Multicenter feasibility study of tumor molecular profiling to inform therapeutic decisions in advanced pediatric solid tumors: The Individualized Cancer Therapy (iCat) study. JAMA Oncology. 2016; 2(5):608–615.
24. Mosse YP, Lim MS, Voss SD, et al. Safety and activity of crizotinib for paediatric patients with refractory solid tumours or anaplastic large-cell lymphoma: A children's oncology group phase 1 consortium study. Lancet Oncol. 2013; 14(6):472–480. [PubMed: 23598171]
25. Gollust SE, Gordon ES, Zayac C, et al. Motivations and perceptions of early adopters of personalized genomics: Perspectives from research participants. Public Health Genomics. 2012; 15(1):22–30. [PubMed: 21654153]
26. Miller FA, Hayeems RZ, Bytautas JP, et al. Testing personalized medicine: Patient and physician expectations of next-generation genomic sequencing in late-stage cancer care. Eur J Hum Genet. 2014; 22(3):391–395. [PubMed: 23860039]
27. Blanchette PS, Spreafico A, Miller FA, et al. Genomic testing in cancer: Patient knowledge, attitudes, and expectations. Cancer. 2014; 120(19):3066–3073. [PubMed: 24962202]
28. Scollon S, Bergstrom K, Kerstein RA, et al. Obtaining informed consent for clinical tumor and germline exome sequencing of newly diagnosed childhood cancer patients. Genome Med. 2014; 6(9):69. [PubMed: 25317207]
29. Oberg JA, Glade Bender JL, Cohn EG, et al. Overcoming challenges to meaningful informed consent for whole genome sequencing in pediatric cancer research. Pediatr Blood Cancer. 2015; 62(8):1374–1380. [PubMed: 25832998]
30. Green RC, Berg JS, Grody WW, et al. Acmg recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med. 2013; 15(7):565–574. [PubMed: 23788249]

31. Parsons DW, Roy A, Plon SE, et al. Clinical tumor sequencing: An incidental casualty of the american college of medical genetics and genomics recommendations for reporting of incidental findings. J Clin Oncol. 2014; 32(21):2203–2205. [PubMed: 24958819]
32. American College of Medical Genetics and Genomics. [Accessed February 16, 2016] ACMG updates recommendation on “opt out” for genome sequencing return of results. Press Release. https://www.acmg.net/docs/Release_ACMGUpdatesRecommendations_final.pdfPublished April 1, 2014
33. Zhang J, Walsh MF, Wu G, et al. Germline mutations in predisposition genes in pediatric cancer. N Engl J Med. 2015; 373(24):2336–2346. [PubMed: 26580448]
34. Ziniel SI, Savage SK, Huntington N, et al. Parents’ preferences for return of results in pediatric genomic research. Public Health Genomics. 2014; 17(2):105–114. [PubMed: 24642506]
35. McCullough LB, Slashinski MJ, McGuire AL, et al. Is whole-exome sequencing an ethically disruptive technology? Perspectives of pediatric oncologists and parents of pediatric patients with solid tumors. Pediatr Blood Cancer. 2016; 63(3):511–515. [PubMed: 26505993]
36. Joffe S, Cook EF, Cleary PD, et al. Quality of informed consent: A new measure of understanding among research subjects. J Natl Cancer Inst. 2001; 93(2):139–147. [PubMed: 11208884]
37. Furr LA, Kelly SE. The genetic knowledge index: Developing a standard measure of genetic knowledge. Genet Test. 1999; 3(2):193–199. [PubMed: 10464667]
38. Gray SW, Hicks-Courant K, Lathan CS, et al. Attitudes of patients with cancer about personalized medicine and somatic genetic testing. J Oncol Pract. 2012; 8(6):329–335. [PubMed: 23598841]
39. Condit CM. Public understandings of genetics and health. Clin Genet. 2010; 77(1):1–9. [PubMed: 20092586]
40. Rew L, Kaur M, McMillan A, et al. Systematic review of psychosocial benefits and harms of genetic testing. Issues Ment Health Nurs. 2010; 31(10):631–645. [PubMed: 20854036]
41. Sugarman J, Lavori PW, Boeger M, et al. Evaluating the quality of informed consent. Clin Trials. 2005; 2(1):34–41. [PubMed: 16279577]
42. Wolfe J, Klar N, Grier HE, et al. Understanding of prognosis among parents of children who died of cancer: Impact on treatment goals and integration of palliative care. JAMA. 2000; 284(19): 2469–2475. [PubMed: 11074776]
43. Mack JW, Cook EF, Wolfe J, et al. Understanding of prognosis among parents of children with cancer: Parental optimism and the parent-physician interaction. J Clin Oncol. 2007; 25(11):1357–1362. [PubMed: 17416854]
44. Gray SW, Hicks-Courant K, Cronin A, et al. Physicians’ attitudes about multiplex tumor genomic testing. J Clin Oncol. 2014; 32(13):1317–1323. [PubMed: 24663044]
45. Coughlin SS. Recall bias in epidemiologic studies. J Clin Epidemiol. 1990; 43(1):87–91. [PubMed: 2319285]
46. Kaphingst KA, Facio FM, Cheng MR, et al. Effects of informed consent for individual genome sequencing on relevant knowledge. Clin Genet. 2012; 82(5):408–415. [PubMed: 22694298]

TABLE I

Demographics and Characteristics

	Number of respondents (%)
Survey respondent	
Patient	11 (24%)
Parent	33 (73)
Other relative/guardian	1 (2)
Time to survey completion (months)	
From enrollment [median (IQR)]	11.6 (19.1, 24.0)
From return of results [median (IQR)]	13.5 (11.2, 18.8)
Respondent age	
<30 years	12 (27)
30–39 years	7 (16)
40–49 years	14 (31)
>50 years	12 (27)
Respondent sex	
Female	27 (60)
Respondent highest education level attained	
High school or less	5 (11)
Some college	14 (31)
College degree	12 (27)
Graduate degree	14 (31)
Respondent race/ethnicity	
White	25 (56)
Hispanic/Latino	7 (16)
Black/African-American	6 (13)
Other	7 (16)
Site	
Boston	29 (64)
San Francisco	6 (13)
New York	5 (11)
Washington, D.C.	5 (11)
Patient age at time of enrollment *	
<2 years	3 (9)
2–5 years	9 (26)
6–9 years	6 (18)
10–13 years	8 (24)
14–17 years	8 (24)
Patient sex *	

	Number of respondents (%)
Female	17 (50)
Received iCat treatment recommendation	
Yes	12 (27)
Received targeted matched therapy	
Yes	1 (2)
Diagnosis	
Ewing sarcoma	5 (11)
Osteosarcoma	3 (7)
Rhabdomyosarcoma	6 (13)
Other sarcoma	12 (27)
Renal tumor	6 (13)
Neuroblastoma	6 (13)
Other	7 (16)
Receiving cancer treatment at time of survey completion	
Yes	21 (47)
Self-reported health status at time of survey	
Excellent/very good	26 (59)
Good/fair/poor	18 (41)
Self-reported likelihood of cure at time of survey	
>80% chance of cure	15 (33)
60–80% chance	11 (24)
40–59% chance	10 (22)
<40% chance	9 (20)
Experience with genetics and/or genetic testing	
Yes	31 (69)

IQR, interquartile range.

*Age and sex is reported for the children of adult survey respondents (n=34)

TABLE II

Participant Hopes/Concerns for and Results of Participation in GTP Research*

Positive themes	Patient/parent recall of hopes at time of enrollment (%)	Patient/parent report of actual benefits received from participating (%)	p-value**
New information about my/my child's cancer	36 (82%)	11 (24%)	<0.001
New information about my/my child's genes	19 (43)	6 (14)	0.008
A greater number of treatment options	31 (72)	12 (27)	<0.001
Peace of mind	21 (48)	9 (20)	0.002
Increased hope for cure for myself/my child	26 (59)	12 (27)	<0.001
Increased hope for cures for future children	39 (89)	25 (56)	<0.001
Negative themes	**Patient/parent recall of concerns at time of enrollment (%)**	**Patient/parent report of actual harms experienced from participating (%)**	**p-value****
Increased stress/anxiety about my/my child's cancer	3 (7%)	0 (0%)	***
Increased stress/anxiety about my/my child's genes	1 (2)	0 (0)	***
Increased stress/anxiety due to new information about my family	3 (7)	0 (0)	***
Loss of insurance or employment	3 (7)	0 (0)	***
Increased stress/anxiety from waiting for results	11 (26)	2 (4)	0.007
Disappointment with results	7 (16)	5 (12)	0.7

GTP, genomic tumor profiling.

* Survey questions available in Supplementary Materials.

** P-values reported for McNemar's exact test.

*** Test statistic could not be calculated due to insufficient number of affirmative responses.

TABLE III

Participant Preferences Regarding Return of GTP Results *

	Would have wanted this type of information reported back (%)		
Cancer-related data	**Overall cohort (N=45)**	**Parent/guardian (N=34)** **	**Patient (N=11)** **
Information that told doctors that the patient was more likely to be cured than previously thought	39 (93%)	28 (90%)	11 (100%)
Information that told doctors that the patient was less likely to be cured than previously thought	23 (56)	17 (57)	6 (55)
Information that directed doctors toward new treatment options based on genetic changes found in the tumor	42 (98)	31 (97)	11 (100)
Information about genetic changes in the tumor that did not suggest a new treatment	34 (81)	26 (84)	8 (72)
Additional data			
Information that told doctors that family members might be at an increased risk of developing cancer	36 (86%)	26 (84%)	10 (91%)
Information that told doctors about a condition other than cancer that could be passed down to your/your child's children	36 (88)	26 (87)	10 (91)
Information about your child's/family's genes or health that would allow doctors to screen for or prevent these conditions	39 (93)	29 (94)	10 (91)
Information about your child's/family's genes or health, but no screening or prevention is available for these conditions	30 (73)	21 (70)	9 (82)
Information about your child's/family's genes or health, but doctors do not know if it would cause any illnesses or conditions	32 (78)	24 (80)	8 (73)
All of the above results	21 (54%)	16 (57%)	5 (45%)

GTP, genomic tumor profiling.

* Survey questions available in Supplementary Materials.

** There was not a statistically significant difference (by Fisher's exact test) between parent/guardian and patient responses for any single item.