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Interest and Attitudes of Patients With Advanced Cancer With Regard to Secondary Germline Findings From Tumor Genomic Profiling

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QUESTION ASKED: How interested are patients with advanced cancer in learning secondary germline findings that arise from the use of tumor genomic profiling, and what do they perceive to be the benefits and harms of this risk information?

SUMMARY ANSWER: Most participants expressed interest in the prospect of learning their secondary germline findings (57%), although a minority was equivocal (29%) or disinterested (14%) in this information. Participants identified a variety of benefits (eg, disease prevention or management, altruism) and harms (eg, emotional harms and distress) that influenced their interest, and these attitudes were uniquely informed by their personal disease experience and health status.

WHAT WE DID: We conducted semi-structured one-on-one interviews with 40 patients diagnosed with advanced breast, bladder, colorectal, or lung cancer who had undergone tumor genomic profiling at our institution and evaluated the qualitative data by using a thematic content analysis approach.

WHAT WE FOUND: Many, but not all, patients with advanced cancer were interested in learning their secondary germline findings arising from tumor genomic profiling. Patients anticipated diverse benefits as well as specific harms from this risk information for themselves, their families, other patients with cancer, and society.

BIAS, CONFOUNDING FACTOR(S), REAL-LIFE IMPLICATIONS: Patients with advanced cancer are presently the principal users of tumor genomic profiling, and a sizeable minority is likely to harbor pathogenic germline variants that could be detected as secondary germline findings. With the growing adoption of tumor genomic profiling, patients with advanced cancer will increasingly be confronted with the decision to learn their secondary germline findings or not; understanding the unique perspectives of these individuals is critical for determining how to optimally support them in this decision-making context. This study provides an in-depth analysis of the perspectives of a small sample of patients with advanced cancer diverse in cancer type, gender, education, and health status who had first-hand experience with tumor genomic profiling at our institution. However, future studies will be needed to determine the interest and attitudes of patients in other care settings and of different cancer stages. Nonetheless, these results have direct relevance for clinicians and researchers involved in precision medicine and cancer care, as they highlight the core values and potential misperceptions that will need to be addressed with educational and decision support interventions for this patient population. JOP

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ASSOCIATED CONTENT

Appendix available online

Abstract

Purpose

Tumor genomic profiling (TGP) can reveal secondary findings about inherited disease risks in a patient with cancer. Little is known about how patients with advanced cancer, currently the primary users of TGP, perceive the benefits and harms of secondary germline findings.

Methods

We conducted semistructured interviews with 40 patients with advanced breast, bladder, colorectal, or lung cancer who had TGP. Qualitative interview data were evaluated by using a thematic content analysis approach.

Results

Most participants expressed interest in the prospect of learning their secondary germline findings (57%), although a minority was equivocal (29%) or disinterested (14%). Reasons for these preferences varied but were influenced by participants' perceptions of diverse benefits and harms of this information, which they regarded as relevant to themselves; their families; and other patients with cancer, medical science, and society. These attitudes were uniquely shaped by participants' personal disease experiences and health status.

Conclusion

Many patients with advanced cancer are interested in learning secondary germline findings and hold optimistic and perhaps unrealistic beliefs about the potential health benefits. Patients also have important concerns about clinical and emotional implications of this information. These perceptions are necessary to address to ensure that patients make informed decisions about learning secondary germline findings.

INTRODUCTION

Tumor genomic profiling (TGP) can identify genetic variants within a patient's tumor that may make the cells susceptible to targeted medications. Currently, TGP is used primarily among patients with advanced cancer to identify eligibility for clinical trials of novel therapeutics.[1,2] Through TGP, germline variants indicative of inherited disease risks may be identified in tumor DNA. Alternatively, the patient's normal DNA may be directly sequenced for comparison with tumor sequence, which potentially reveals germline variants that indicate inherited risks for health conditions with differing severity, treatability, likelihood of development, and relevance for the patient's

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health.[3-5] These germline findings are considered secondary when actively sought (or incidental when not) because they arise outside the original purpose of TGP.[6,7] Experts are debating how to ethically and practically manage such germline findings,[8-11] with the American College of Medical Genetics and Genomics currently recommending that patients be allowed to opt out of receiving secondary germline findings (SGFs).[12-14] Research is needed to examine patients' perspectives about the discovery, disclosure, and management of SGFs to ensure that their preferences are addressed adequately.[7,15]

Several studies have demonstrated that patients with varying stages of cancer are interested in the hypothetical[16-18] and real[19] prospect of learning this risk information gained from TGP. Little is currently known, however, about patient attitudes that contribute to this interest. This issue is particularly critical for patients with advanced cancer who generally face poor prognoses and are thus likely to receive limited clinical benefits from learning SGFs about their future disease risks. The few existing qualitative studies with patients and family members identified an enhanced ability to plan for the future[20] and family obligations[21] as important reasons to receive germline results, yet patients were concerned about the burden of this information.[20,21] There is a need to better understand how patients with advanced cancer perceive the benefits and harms of SGF, as this could allow health care providers to optimally support patients as they make decisions about whether to learn this information or not.

To address this gap in knowledge, we used qualitative semistructured interviews to collect in-depth narratives from patients with advanced cancer who had TGP at our institution. These individuals were informed about the possible incidental discovery of germline variants through the TGP consent process, but at the time of this study, our institution did not routinely conduct secondary analyses. Therefore, these patients had direct experience with TGP and awareness of the issue of potential germline variants but had not made a definitive decision about learning SGFs. We assessed their perceptions of the benefits and harms of learning SGFs as well as of how these attitudes shaped their personal interest in receiving this risk information.

METHODS

Recruitment and Participants

At the time of this study, patients with late-stage solid tumors could undergo TGP with the MSK-IMPACT (Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets) test,[22,23] a sequencing panel that detects somatic variants in 410 cancer-related genes with analysis of a matched normal sample and germline subtraction, through an institutional research protocol; study participants were recruited from those enrolled in this protocol. Eligible patients were those with breast, colorectal, bladder, or lung cancer; age 18 years or older; New York metropolitan area residents (two were recruited outside this area to meet our target distribution of sex and cancer type); and healthy enough to be approached about the study as determined by their physicians. The MSK Cancer Center institutional review board approved this study.

To obtain a breadth of participant perspectives and remain consistent with recommended qualitative research guidelines for thematic saturation,[24] we aimed to recruit 40 patients—10 female patients with breast cancer, 10 patients with colorectal cancer (five female, five male), 10 patients with bladder cancer (five female, five male), and 10 patients with lung cancer (five female, five male). A research assistant approached 66 eligible patients during a clinic visit or mailed a recruitment letter with a subsequent telephone follow-up; of these patients, 18 actively or passively declined participation, and eight could not be contacted by telephone.

Data Collection and Analysis

We used qualitative methodology, which is well suited for exploratory and evaluative research in understudied areas and generates findings that can be investigated further in quantitative studies.[25,26] Specifically, we conducted individual semistructured interviews.[27-30] Our multidisciplinary research team developed an interview guide consisting of exploratory questions designed to elicit participant perspectives. Two team members conducted interviews in person or by telephone on the basis of participant preference. All participants provided informed consent before the interview. Interviews lasted approximately 45 minutes and were audio recorded and transcribed. Limited demographic data were collected in the interview and abstracted from participants' medical records. Participants received a $25 gift card in appreciation for their contribution.

Transcripts were analyzed through thematic content analysis, an inductive qualitative data analysis method that identifies and interprets recurring conceptual patterns directly from the data through intensive reading, coding, and interpretation.[28,29,31-33] This gold standard analytic approach[27,29] included the use of four coders to achieve analyst triangulation[34]

and iterative rounds of consensus analysis to ensure trustworthiness of the findings.[35] ATLAS.ti software was used to facilitate analysis.[36] We selected illustrative participant quotes from the interview data to support our findings and computed descriptive statistics for demographic data.

RESULTS

Participant Characteristics

Participants' characteristics are listed in Table 1. The majority had stage IV disease (92.5%), and one third (32.5%) self-reported as being fully active and capable of all predisease physical activities. Participants were predominantly white (85%), were married or partnered (87.5%), and had children (70%). Participants did not differ from decliners (n = 26) in age, cancer, race, or clinical trial status; however, women were more likely to participate (P = .005).

Interest in SGFs

When asked to imagine that SGFs arising from their use of TGP were now available, the majority of participants (57%) expressed interest in this information. However, many were equivocal about their current interest (29%), and a minority expressed disinterest (14%). Reasons for these preferences varied but were influenced by participants' perceptions of the benefits and harms of this information as well as their experiences associated with their present health status. These attitudes are described in the next sections.

Perceived Benefits and Harms

Participants articulated a number of potential benefits and harms associated with learning their SGFs. Participants perceived that three different groups may experience these outcomes: the individual patient; family members; and other patients with cancer, medical science, and society (Appendix Fig A1, online only). We describe the various benefits and harms that participants identified as relevant for each group (key themes indicated by italicized text; illustrative participant quotes listed in Table 2).

Individual patient

Participants identified three primary benefits of SGFs for themselves. First, many placed a *high value on being informed* and noted that "knowledge is power." Many believed that the ability to learn any information relevant to their present or future health is an obvious benefit. A second benefit involved the opportunity for *life planning and preparation for the future*. Participants primarily associated this benefit with non-actionable SGFs (ie, indicating risk for a disease without effective treatment, one's status as a healthy carrier of a disease-causing mutation). They believed that such risk information could inform life decisions about reproduction or help them to prepare for the possibility of serious, incurable conditions (eg, Alzheimer's disease). A related benefit was *disease prevention or management*; although several participants anticipated that this information could improve their current cancer treatment, many more described the possible identification of treatment options for other diseases for which they may be at risk, early detection of future diseases, and improved motivation for adopting healthy behaviors.

Approximately one half of participants (53%) did not anticipate that they would directly experience any harms upon learning their SGFs. However, some believed that learning this information would cause them *emotional harms and distress*. For example, participants believed that they could experience stress about whether their current lifestyle behaviors would increase their disease risks, and anxiety upon learning that family and future generations could be at risk. A few participants also anticipated harms associated with *privacy or the misuse of information*. These individuals noted that information to be gained from SGFs is private, and there are risks to how institutions or groups (eg, insurance companies, employers, government) may mishandle it.

Family members

Participants identified benefits of their SGFs for nonbiologic and biologic family. For nonbiologic family members (predominantly spouses and partners), knowledge of this *information would help them to care for the patient*; for example, it could enhance understanding of the patient's health and enable family to optimally support the patient. Participants also anticipated that by becoming aware of the utility of TGP and their SGFs, both nonbiologic and biologic family members could benefit from an increased *awareness and use of genetic testing*. Finally, a majority of participants expected that for biologic family members (primarily children and siblings), their SGFs could prompt *disease prevention or management*. Biologic family members could make more-informed decisions about their current and future health, such as engagement in preventive or surveillance behaviors.

Emotional harms and distress was the primary harm that participants identified for their families. Some anticipated that

Table 1. Participant Characteristics

Characteristic	No. (%)
No. of participants	40
Age, years	
Mean ± SD	58.8 ± 12.8
Range	30-82
Female sex*	25 (62.5)
Race	
White	34 (85.0)
Black	1 (2.5)
Asian	4 (10.0)
Refused	1 (2.5)
Hispanic ethnicity	2 (5.0)
Educational attainment	
Less than high school	1 (2.5)
High school graduate	4 (10.0)
Vocational/technical school	1 (2.5)
Some college	11 (27.5)
College graduate	7 (17.5)
Postgraduate	16 (40.0)
Marital status	
Married or partnered	35 (87.5)
Divorced or separated	0 (0)
Widowed	3 (7.5)
Single	2 (5.0)
Parental status (has children)	28 (70.0)
Cancer type	
Bladder	10 (25.0)
Breast	10 (25.0)
Colorectal	10 (25.0)
Lung	10 (25.0)
Stage IV cancer	37 (92.5)
Self-reported health status†	
Fully active, able to carry out all predisease performance without restriction	13 (32.5)
Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (eg, light house work, office work)	23 (57.5)
Ambulatory and capable of all self-care but unable to carry out any work activities, up and about for > 50% of waking hours	4 (10.0)
Capable of only limited self-care, confined to bed or chair > 50% of waking hours	0 (0)
Completely disabled, cannot carry on any self-care, totally confined to bed or chair	0 (0)
Actively enrolled in a clinical trial	18 (45.0)

*An equal number of women (n = 5) and men (n = 5) were interviewed for each cancer type, with the exception of breast cancer for which all participants were women (n = 10).
†As assessed with the single-item Eastern Cooperative Oncology Group performance status.[37]

this risk information could generate intense fear, anxiety, and perhaps fatalistic thinking about the likelihood of developing disease. A few participants believed that this information could be particularly emotionally burdensome for their parents.

Other patients with cancer, medical science, and society

Participants described several benefits of SGFs most relevant to individuals separate from themselves and their families. Some believed that their SGFs could ultimately *improve cancer treatment options* for other patients. They anticipated that this information could help to identify cures and treatments, enhance quality of life, and extend patients' lives. In addition, participants anticipated that their SGFs could *advance medical knowledge* by contributing to valuable scientific research. Finally, some described benefits that reflect a sense of *altruism*. These participants believed that their SGFs could lead to general societal benefits associated with "paying it forward" to future generations in terms of identifying improved health and disease management options, despite a belief that they themselves would not accrue such benefits from this information.

Participants identified harms that they believed were most applicable to other patients with cancer who may receive SGFs. Several participants acknowledged that SGFs represent *uncertain, probabilistic information* that may be inaccurate and complicate others' decision making about how to best manage their health. Consequently, other patients could overreact to this information and engage in overtreatment or interventions that would negatively affect their quality of life (eg, prophylactic surgeries, pregnancy terminations). Similarly, a few participants described how the uncertainty of SGFs could lead to *limited clinical utility* for other patients. For instance, upon learning their SGFs,

Table 2. Perceived Benefits and Harms of Learning Secondary Germline Findings* and Illustrative Participant Quotes

Benefit/Harm	Illustrative Quote
Individual patient	
Benefits	
Value of being informed	"I think any information you can learn about your health, if it could be good or bad, it's still good because I really feel you should be aware. I think people need to be aware. So I guess my answer is, no, there wouldn't be anything that would be detrimental to learning that." (F/LC)
Life planning and preparation for the future	"If you've ever had a disease or ever had something that's, that runs in the family, you know that knowing is, is a whole lot better than not being aware, or not being ready, or just a lack of knowledge is, is not to your benefit. You definitely want to know because…it just helps you, you know, psychologically and physically, and—and like I said, it's preparation. You don't, you don't realize that until you've been in this situation, but preparation's a good thing." (F/BrC)
Disease prevention or management	"If there was a, mutation that gave a high probability of developing a particular disorder, surveillance could start early, and there could be early diagnosis and early treatment that would be very helpful." (F/LC)
	"Change of diet perhaps. I mean, yesterday somebody mentioned hypertension or if your genes show proclivity to hypertension, then I might change my diet or exercise or things like that or go to the doctor. And if I find I have a proclivity to diabetes, stop eating sugar." (F/BrC)
Harms	
Emotional harms and distress	"Can you imagine thinking that you have cancer or in the future my daughter is going to get cancer? That's not a good feeling. That's not a comfortable feeling, you know? But I mean if it's a fact, what can you do about it? There's nothing you can do about it except just feeling uncomfortable." (F/BlC)
Privacy or misuse of information	"And then I don't know if that information being available to like insurance providers and stuff can actually be detrimental to your coverage and stuff." (M/BlC)
Family members	
Benefits	
Nonbiologic family: information to help care for the patient	"My husband more because he's in this with me. He travels this journey and has to deal with everything I go through, positive and negative. So him more because he's my support, right? So he would help me deal with it. He would help me get to the doctors, get to the medicine, both emotionally, spiritually, physically, financially, right? So he'd be my enabler in the best sense of the word, right?" (F/CC)
Nonbiologic family: awareness and use of genetic testing	"And it might affect [my husband] in wanting to be tested also to find out if there's anything in particular that he can intervene with, you know, in his own genetic background, because he has his own family history and things like that. So he might be interested in being tested if there was such a test to do that." (F/CC)
Biologic family: awareness and use of genetic testing	"If there's other diseases or illnesses that could be treated. I guess potentially if I have other hereditary stuff, then other people in my family can be tested and treated before anything would become an issue." (M/CC)
Biologic family: disease prevention or management	"It helps [my family members'] own lives. You know, it helps them—basically they're part of me, so it helps them in their future, in their own health, and, you know, that's it. Well, if there's something to prevent or if there is something they can change about their lifestyle, they can do it." (F/BlC)
Harms	
Emotional harms and distress	"I see me calling my brother and saying to him, 'Wow, my genes say it's 90% sure that we're going to get pancreatic cancer,' you know, and he's got two young children. Now I've not only introduced fear for himself of not being around for his kids but fear of his kids dying of cancer into his and his wife's life." (F/CC)
	"[My mother] would just worry. I mean she's 97. I don't really think at this stage she needs to know…because it's just…too much for her to hear and she would be very, very upset over it." (F/BrC)

(continued on following page)

Table 2. Perceived Benefits and Harms of Learning Secondary Germline Findings* and Illustrative Participant Quotes (continued)

Benefit/Harm	Illustrative Quote
Other patients with cancer, medical science, and society	
Benefits	
Improve cancer treatment options	"I just think possibly you could maybe help somebody else down the line and if nothing comes up in my lifetime, maybe in somebody else's lifetime there'll be some kind of—if you find something wrong that maybe a medicine could change it, or like I said, prolong. The more you prolong life and—like a good, you know, good quality of life, that's how—that's why I believe in doing it, just to hopefully learn more about the disease." (F/BrC)
Advance medical knowledge	"Not just for me, but again, at the point in my life where, not to be altruistic or whatever, but it might persist in being part of a larger group that would help the medical community along, research along." (M/LC)
Altruism	"My attitude is that I want them to use every blood test and every cell of the tumors from the operation that they can to help future generations and my—like I didn't think, and they didn't think at the time that we talked about it, that they would find anything useful in time to help me in my disease. So when I think about it I think about it really for future generations and less for my family, you know, or me." (F/CC)
Harms	
Uncertain, probabilistic information	"I'm sure it could scare the hell out of people because it is, after all, still in its infant stages, and so many people might be scared that, you know, what if I do have this potential mutation? Does this mean I'm definitely going to get it? And there's so many other things that could cause cancer and do things to cancer and trigger cancer that we still don't know." (F/CC) "The possibility of false results….One always hopes for 100% accuracy, but that isn't always the case in medical situations." (F/LC)
Limited clinical utility	'Well not for me. I do think there are people in the general public who could get really confused….I think people could end up paying for things that are not useful for them, and I know research studies would not charge, but you know what I mean?...Once people started talking about how you could get this information, I think people misunderstand and now pay for things that aren't going to be useful to them and it's just—yeah, I do think it has a danger of turning into a rip-off or a health care rip-off." (F/CC)
Emotional harms and distress	"Well, I would think that they might go in the wrong direction and say, 'Oh my, oh my, oh my, this...could mean that I'm going to not be able to bear children,' in the case of a woman, for example. Or, 'This might be—I will not be able to do so many other things, I may not be able to see well after age 50.' Who knows? They might go crazy with that information. I can understand that." (M/BlC) "I don't think I would have a bad reaction to it, but there may be people who just don't want to know or would be frightened. The development of a disease isn't necessarily certain, I would think, and yet that might frighten people….They're going to wake up every day thinking that today is the day I'm going to have symptoms of something that, you know, was a possible development. So I guess it would depend a lot upon the individual person and how they would react to that information psychologically." (M/CC)

NOTE. Participant characteristics are denoted after each quote as sex/cancer type.

Abbreviations: BlC, bladder cancer; BrC, breast cancer; CC, colorectal cancer; LC, lung cancer.

*The interview guide described secondary germline findings as follows: "With tumor genomic profiling, sometimes the lab will also look for mutations in the genes in your normal cells. Although the lab at MSK [Memorial Sloan Kettering] is not looking for mutations in the genes in your normal cells, let's imagine what would happen if a lab did. The lab could find mutations in the genes in your normal cells that mean different things. The meaning of some of these mutations is currently unknown, but other mutations could be associated with many different disease risks for you. These mutations would likely be something that you were born with. Because mutations in genes in your normal cells could be inherited or passed on, they could also affect the health of your family."

patients with cancer may pay for unnecessary testing and interventions that may not be personally useful, which would lead to inappropriate health care utilization and costs.

The prospect of *emotional harms and distress* was most often described as relevant for other patients with cancer. Participants believed that if other patients received SGFs, they may experience anxiety and attribute a higher degree of

certainty to the risk information than is appropriate or realistic. Participants identified characteristics that might place one at greater risk for experiencing emotional distress, including being younger, being prone to anxiety, and having limited effective coping strategies.

Unique Perspectives as Patients With Advanced Cancer

Participants considered their present medical and personal context, which included their diagnosis of advanced cancer, age, and life stage, when assessing the prospect of learning SGFs (Table 3). These factors appeared to directly inform participants' attitudes about the value of health risk information. For some, receipt of an unexpected cancer diagnosis and the challenges of treatment consequently led them to place great *importance on the possibility of being prepared for other diseases*. Some participants articulated a link between their cancer diagnosis and their *belief that any knowledge is worthwhile*, strongly valuing the receipt of their SGFs regardless of whether this information had any negative implications. Yet a number of participants, on the basis of their disease severity and older age, also recognized that they may not derive significant direct benefits from learning their SGFs (eg, "It's too late for me"). However, many expressed a *desire to help others* by acknowledging the value of this information for family and society.

Similarly, participants' experiences as patients with advanced cancer influenced their attitudes about the emotional harms that could arise from learning their SGFs. Two distinct perspectives emerged with regard to their own emotional capacity. First, some participants believed that they had already met their own threshold for learning negative health information and expressed *concern about their emotional capacity*. As such, learning SGFs could be "too much" to manage after having contended with cancer. However, others expressed *confidence about their emotional capacity* because they already possessed the fortitude to manage distress associated with a terminal cancer diagnosis. These individuals expressed confidence in their ability to manage any distress that might come from learning their SGFs, which may pale in comparison with that associated with their cancer diagnosis.

DISCUSSION

Patients with advanced cancer are presently the principal users of TGP,[1,2] and a sizeable minority is likely to harbor pathogenic germline variants that could be detected as SGFs; for example, presumed pathogenic germline variants were observed in 15.7% of patients tested with the MSK-IMPACT test.[38] Exploration of the unique perspectives of these individuals is a critical step toward determining how to best support patients while they decide whether to learn SGFs. Consistent with studies conducted with patients with cancer in various settings,[16-19] we found that a majority of participants with advanced cancer who had previously undergone TGP were interested in the prospect of learning their SGFs. Yet many felt unsure or disinterested in this information. Furthermore, participants considered both the potential benefits and the potential harms when assessing the value of SGFs, which suggests that these perceptions strongly influence patients' interest in receiving this risk information.

We observed that participants held generally optimistic views of the benefits of SGFs for themselves, including the benefits of being informed and able to prevent and prepare for future health challenges. However, it is important to recognize that some of these anticipated benefits may be unrealistic for many patients given their advanced disease status and poor prognosis. To ensure that patients with advanced cancer make fully informed decisions about the receipt of SGFs, health care providers must devote attention to helping these patients to accurately understand their prognosis and the limited likelihood of deriving direct health benefits.

Participants anticipated little harm for themselves in response to SGFs. Their greatest concerns were related to emotional distress, although this was perceived as being most applicable to others, including family and other patients with cancer. Research has confirmed that genetic testing for cancer predisposition generally has a limited impact on emotional distress,[39,40] but little is known about how patients with cancer who are facing the end of life may respond to this information. Participants noted two potential options reflecting either emotional resilience or emotional overload. Such anticipated responses not only support the importance of allowing patients to opt out of the return of SGFs[12] but also highlight the need for future research to examine the diverse ways in which patients with advanced cancer may emotionally respond to and cope with inherited risks revealed by TGP.

Most participants anticipated a number of highly valued potential health benefits of learning their SGFs for individuals beyond themselves, including biologic and nonbiologic family. Yet, participants expressed concerns about their families experiencing distress and were particularly concerned about the disclosure of information to their parents, which may be a

Table 3. Influence of Participants' Experiences With Advanced Cancer Upon Their Attitudes About Secondary Germline Findings and Illustrative Quotes

Reason/Attitude	Illustrative Quote
Reasons for valuing information	
Importance of preparation for other diseases	"And I think that should run true for anybody who's—whether it's Alzheimer's or diabetes, or—if you think you might have a possibility of getting this here, wouldn't you want to know? Wouldn't you want to be prepared? Wouldn't you want to also find out what's out there so that maybe it could help you or you sort of find out what the benefits are? I don't know, that's just me, I just, that's just how I feel. I want to know. If I could have prevented this [cancer] here, I would of; I would have been the first one." (F/BrC)
Belief that any knowledge is worthwhile	"It's interesting to me that, you know, I'm 67 years old, so I suspect it's possible that how I feel today will be different than I would have felt 30 years ago or 40 years ago. I'm at the point in my life where I think there probably isn't such a thing as too much knowledge. And I'm being treated for, you know, for this cancer and other issues, so I don't think anything would be piling on." (M/LC)
	"But I don't mind, since I'm already terminal I'd like to have all the information, positive or negative….It very likely, in my opinion, wouldn't impact my life in any way because I already know I have a terminal disease, so I would want to know just out of an intellectual curiosity." (F/CC)
Desire to help others	"I'm in favor of. Whether it helps me or not, I don't, you know, I don't know…I'm 80 years old, okay, so…you know, I'd love to live another 20 years, but I don't know what the likelihood of that is. But if it helps my children and their children, then of course I'm interested in doing it." (F/BlC)
Attitudes about emotional harms and distress	
Concern about emotional capacity	"It could be useful, but it also could be potentially very hard for people, very devastating, particularly if they're getting it in the process of, you know, they already have cancer. That's, you know, like it's not like you just went in and said, 'Do my genes profiling.' It's because you already have cancer. So you already have a serious disease and I'm not sure that finding out that you might get yet another serious disease is a piece of information that would be useful unless there were some specific thing you could do to prevent that other disease from happening." (F/CC)
	"It's sort of enough right now to know that I have cancer….I sort of feel like I would be upset to learn that I was, for example, at a very, very high risk for some other dreadful disease, like Parkinson's or something like that, you know. So part of it is that and part of it is that I'm not sure that there are ways to act on that information given how old I am. You know, preventative kinds of things, you know, like you should have been living all these years with not eating so much meat, stuff like that, you know. So I'm not sure that there's a way to act on the information. So it's a combination. It's both the emotional stress of taking on another serious disease or the fear of another disease, and it's also just the practical inability to put to work sort of preventative strategies when you're as old as I am." (F/CC)
Confident about emotional capacity	"I think it's always a benefit to learn of potential what you—what your genes—what you're carrying. I don't see it as a negative. I know for myself, after being diagnosed with cancer I—nothing—it doesn't scare me if there's some information that is found secondary. I don't see a potential harm…I think it would be a benefit." (F/BrC)

NOTE. Participant characteristics are denoted after each quote as sex/cancer type.
Abbreviations: BlC, bladder cancer; BrC, breast cancer; CC, colorectal cancer; LC, lung cancer.

result of the older age of this sample (median, 59 years). Many expressed a strong desire to help other patients, medical science, and society, with a belief that learning their SGFs would allow them to contribute to scientific knowledge. However, this belief may reflect an important misperception: it is unlikely that patients would be required to agree to receive their SGFs for their biospecimens to be used in medical research. Educational interventions may be needed to ensure that patients understand such distinctions when they consent to both TGP and the receipt of SGFs.

This study has several notable strengths. The qualitative study design allowed for an in-depth analysis of the perspectives

of a small sample of patients with advanced cancer that is diverse in cancer type, sex, education, and health status. However, this sample was racially and ethnically homogenous and obtained from a single institution. Thus, these findings may not be generalizable to the broader population of patients with advanced cancer treated in other care settings who are grappling with the decision to receive SGFs. Future work should examine decision-making processes as patients are increasingly presented with the option of learning SGFs and should explore how patients in other settings and with different cancer stages engage with TGP. All participants had direct experience with TGP, although their consideration of the receipt of SGFs was hypothetical. Furthermore, interviews focused on the possibility of learning SGFs that are pathogenic (reflecting both actionable and nonactionable risk information). However, estimates suggest that most patients (approximately 84%) will not receive meaningful germline information from TGP.[38] How patients may respond cognitively, emotionally, or behaviorally in this situation is unclear. We also did not explicitly assess participants' attitudes about the possibility of SGFs reflecting variants of uncertain clinical significance, although many expressed concerns about the uncertain, probabilistic nature of genetic risk information in general. Future studies should explore patients' experiences with these types of SGFs as TGP is increasingly adopted.

In conclusion, these results demonstrate that many, but certainly not all, patients with advanced cancer are interested in learning their SGFs from TGP. Patients anticipate diverse benefits for themselves and their families as well as for other patients with cancer and society, yet many have serious concerns about the emotional and clinical implications of this information. Furthermore, these patients have unique needs and expectations given their disease experiences, prognosis, age, and life stage, which appear to be important in shaping their perspectives. These results have direct relevance for clinicians and researchers involved in precision medicine and cancer care because they highlight the core values and potential misperceptions that need to be addressed with educational and decision support interventions for this patient population. By addressing these issues, patients with advanced cancer could make truly informed decisions about learning SGFs. JOP

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Interest and Attitudes of Patients With Advanced Cancer With Regard to Secondary Germline Findings From Tumor Genomic Profiling

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Appendix

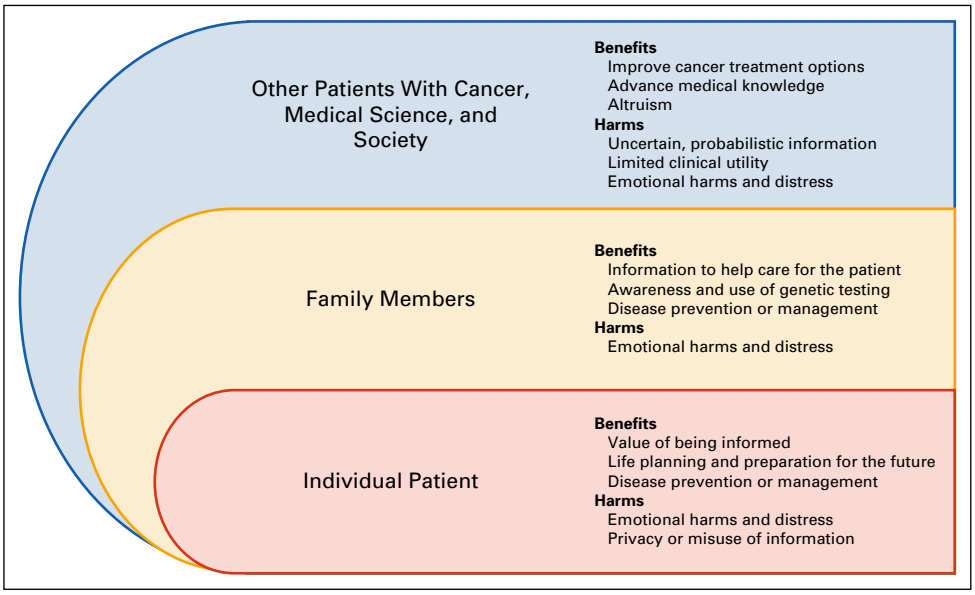

Fig A1. Study results about perceived benefits and harms of learning secondary germline findings from tumor genomic profiling of patients with advanced cancer as categorized into three groups that may experience these outcomes.