original report

Decision-Making Preferences About Secondary Germline Findings That Arise From Tumor Genomic Profiling Among Patients With Advanced Cancers

abstract

Purpose In patients with advanced cancers, tumor genomic profiling (TGP) can reveal secondary germline findings (SGFs) with regard to inherited disease risks. This study examined the process by which patients with advanced cancers would decide about whether to learn these SGFs and their preferences about specific challenging decision scenarios, including whether patients should be required to receive SGFs and whether SGFs should be returned to the family after a patient's death.

Patients and Methods We conducted qualitative semistructured interviews with 40 patients with advanced breast, bladder, colorectal, or lung cancer who had undergone TGP. Data were collected on participants' perspectives about the hypothetical decision to learn their SGFs, including their anticipated approach to the decision-making process, and their preferences about challenging decision scenarios. Data were evaluated by thematic content analysis.

Results We identified themes with regard to participants' preferred degree of decisional autonomy, perceived vital role of doctors, information needs, and anticipated process of deliberation. Although participants reported that this decision was ultimately their own, many wanted input from family and trusted others. Oncologists were expected to provide decision guidance and key clarifying information. Most participants stated that patients should be able to make a choice about receiving actionable SGFs, and a majority stated that SGFs should be available to family after a patient's death.

Conclusion These results provide insight into SGF decision-making processes of patients with advanced cancers, which can allow clinicians to provide patients with optimal decision support in this context. Patients with advanced cancers have specific information needs and decision-making preferences that educational and communication interventions should address to ensure that patients make informed choices about learning SGFs.

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INTRODUCTION

Tumor genomic profiling (TGP) is revolutionizing cancer care. TGP involves the sequencing of somatic DNA to identify genetic variants indicative of tumor susceptibility to targeted therapeutics. TGP also can identify germline variants that indicate inherited disease risks detected either in the somatic DNA or through germline DNA directly sequenced for comparison with the somatic sequence. These germline variants are considered secondary findings when actively sought by researchers or clinicians (or incidental findings when not) because they arise outside the original purpose of TGP.[1,2] Secondary germline findings (SGFs) that indicate risks for various health conditions are likely to be detected in a sizable minority of patients who receive TGP; for example, presumed pathogenic germline variants have been observed

in 15.7% of patients who receive TGP at our institution.[3]

Current American College of Medical Genetics and Genomics recommendations state that individuals who undergo clinical genomic sequencing should be allowed to opt out of receiving SGFs.[4] This recommendation plus the increasing adoption of TGP in clinical care ensure that many patients with cancer will be confronted with the decision about whether to learn their SGFs. This decision is likely to be challenging, particularly for patients with advanced cancers who are currently the primary users of TGP (because of its utility for identifying eligibility for clinical trials of novel therapeutics[5,6]). These individuals must choose whether to learn information about their future disease risks and potential shared familial risks while facing a poor prognosis and the psychosocial challenges of a terminal diagnosis.[7] Although patients with varying stages of cancer have reported interest in receiving such information from TGP in real[8] and hypothetical[9-11] settings, how patients decide whether to learn SGFs is unclear. Understanding the decision-making processes of patients with advanced cancers would allow clinicians to anticipate patient informational and decision support needs in this context.

The current study describes processes by which patients with advanced cancers decide whether to learn SGFs that arise from TGP. We analyzed qualitative data collected through an investigation of attitudes about SGFs among patients who received TGP at our institution.[12] These patients were informed about the possible incidental discovery of germline variants during TGP consent conducted by their primary medical oncologists; however, because our institution did not routinely conduct secondary analyses at the time of this study, none of the patients had made a definitive decision about learning their SGFs. We examined patients' perspectives with regard to factors influential to their hypothetical decision about learning SGFs and preferences about their role in this decision-making process. We also assessed preferences with regard to specific challenging decision scenarios, including whether patients should be required to receive SGFs and whether SGFs should be returned to the family after a patient's death.

PATIENTS AND METHODS

Study methods are described in detail elsewhere.[12] In brief, we recruited 40 adults with advanced breast, bladder, colorectal, or lung cancer who had undergone TGP with an institutional somatic sequencing panel (MSK-IMPACT [Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Targets][13,14]). The Memorial Sloan Kettering Cancer Center institutional review board approved this study.

Individual semistructured interviews[15-18] were conducted with participants 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. Demographic data were collected in the interview and abstracted from medical records. Participants received $25 for their contribution.

Transcripts were analyzed through thematic content analysis, an inductive qualitative data analysis method that identifies recurring conceptual patterns directly from the data through intensive reading, coding, and interpretation.[16,17,19-21] We used four coders to achieve analyst triangulation[22] and iterative rounds of consensus analysis to ensure trustworthiness of the findings.[23] ATLAS.ti was used to facilitate analysis.[24] We selected illustrative participant quotes from the interviews to support our findings and computed descriptive statistics for demographic data.

RESULTS

As listed in Table 1, study participants predominantly had stage IV cancer (92.5%); were white (85%), college graduates (57.5%), married/partnered (87.5%); and had at least one child (70%). Participants described how they would approach the decision if their doctor were to present the option of learning SGFs. We categorized participant responses into four key themes and relevant subthemes (indicated by italicized text); illustrative quotes appear in Table 2.

Theme 1: Degree of Decisional Autonomy

As participants considered how they would decide whether to learn SGFs, a spectrum emerged with regard to participants' preferred degree of decisional control and autonomy from close others. The close others that participants referred to

Table 1. Participant Characteristics

Characteristic	No. (%)
No. of patients	40
Age, years	
Mean ± standard deviation	58.8 ± 12.8
Range	30-82
Female sex*	25 (62.5)
Race	
White	34 (85.0)
Black/African American	1 (2.5)
Asian	4 (10.0)
Refused	1 (2.5)
Ethnicity (Hispanic)	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)
Cancer stage (stage IV)	37 (92.5)
Self-reported health status†	
Fully active; able to carry on 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	23 (57.5)
Ambulatory and capable of all self-care but unable to carry out any work activities; up and about > 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)
Clinical trial status (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 except for breast cancer, for which all participants were women (n = 10).
†As assessed with the single-item Eastern Cooperative Oncology Group performance status.[25]

primarily were significant others, close biologic family members (eg, siblings, children), and occasionally friends. One group of participants expressed a preference for the *patient as an autonomous decision maker*. These participants reported that they would prefer to make the SGFs decision on their own and neither needed nor desired input from others. Influential factors for this perspective included a view that the decision was "my choice" because it involved highly personal information fundamentally related to "my body" and a desire to avoid burdening others, particularly family, with potentially distressing information.

A second group of participants preferred that *close others play a consultative role in the decision-making process*. These participants anticipated communicating with close others about the option to learn SGFs and would consider their advice and opinions but would ultimately make the final decision on their own. Some in this group noted that their family's views were highly valued but would not be determinants in their decision making.

Finally, a smaller group preferred that *close others serve as active partners in decision making*. These participants wanted their close others, particularly spouses/partners, to engage as full collaborators in the SGFs decision. Participants noted that as with other important life decisions, their spouses/partners naturally would be involved in this process. Others explained that their family members should be actively involved in this decision because SGFs may have direct health-related implications for them.

Participants who anticipated the involvement of others in their decision making also described their *process of selecting close others for communication* about the option of learning SGFs. Many participants would seek the perspectives of individuals (eg, siblings, children) who possess medical or scientific expertise. Participants also considered the intimacy of the relationship as well as the individual's level of involvement in their overall health care. Finally, several participants deemed important the ability or appropriateness of the individual to participate in a discussion about this issue, which could depend on the individual's age, cognitive ability, or capacity to cope emotionally with learning negative or upsetting information.

Table 2. Decision-Making Process and Preferences Regarding Secondary Germline Findings and Illustrative Participant Quotes

Theme	Participant Quote
Theme 1: degree of decisional autonomy	
Patient as an autonomous decision maker	"Well, I think that would be up to me to decide, so I wouldn't be asking my family what they think about doing that. I would just say I would make my own decision about that to begin with. That's where it starts." (F/CC)
Close others play a consultative role in the decision-making process	"Well, I'd like their input, but ultimately, I make the decisions for what...kind of treatment....I would make the final decision. It's my body....I'll take their input, but other than that...I'm going to make the decision whether or not to proceed with whatever." (F/BrC)
Close others serve as active partners in decision making	"I would expect my wife to be involved....I trust her knowledge and judgment in these matters. So she'll be in a better position to help me make a decision... about...find[ing] out the outcome of the research and also to help manage it differently if I have an option to. [She would] be a partner in that decision making." (M/BlC)
Process of selecting close others for communication	"I don't think they should be involved in the decision. And it is very peculiar to my situation. I don't think my husband could deal with it, so I don't want him burdened with it, and I don't think my step-kids have enough...skin in the game, so to speak, that they should actually be involved in making the decision… and I guess I feel similarly about sisters and brother that that's too distant. [It] wouldn't make sense for them to be a part of the decision-making process." (F/CC)
Theme 2: vital role of doctors	
Nature and quality of the doctor-patient relationship	"Believe me, it's been a rough road, and so like I said, my oncologist and I, we have a good understanding. And so far, he's steered me in the right. He was the one that put me in the tumor profiling and also on this new research, and anything he decides with me, I'm okay with it because we have that doctor-patient trust. You know, so if he agrees with it, I'm with him. He hasn't steered me wrong yet." (M/BlC)
Primary source of relevant and valuable information	"No, I think my doctor would be enough. He's the only one who really knows my condition, you know?...If he felt it was important, I do whatever they tell me at Sloan. I mean, you know, if they tell me to go get this test, I go get that test....I do it because I think it's in the interest of my health.…You know, you would have to make a strong argument for that case, but if he was insistent, I would do it." (M/BlC)
Theme 3: information needs	
Clinical benefit	"I think from a personal standpoint I would ask...how realistic do you think, or how probable do you think, something that came up as high risk is likely to happen, or is there anything I can do to prevent it? I mean, it's more so in the latter that I would care about more if there's anything I can do to prevent it, to minimize the risk." (M/CC)
Assistance in interpreting meaning	"Well, I guess I would want the doctor to explain to me what mutations might mean. Is it certain mutations, is it only certain diseases that we're talking about, or...is it kind of open ended?...I guess I would want to learn more and hear more about the science of what the mutations might mean." (M/CC)
Degree of scientific uncertainty	"What I'm trying to have connection with is that if this testing were predictive of something, they would be more interested than if [with] this testing, nobody understood or knew how to interpret the results. So I guess it would be depending [on] how far along the continuum we are in being able to use this information [that] would make a difference." (M/LC)
Testing procedure	"Yes, and if it's nothing invasive and they won't...poke me anymore and they won't do anything to me, it's fine with me....I would like to know. But if there is any surgical thing involved or any invasive anything involved, I don't want to do it because I have been through a lot." (F/BlC)

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Table 2. Decision-Making Process and Preferences Regarding Secondary Germline Findings and Illustrative Participant Quotes (Continued)

Theme	Participant Quote
Who will have access	"Who would have that information, would health care providers...have to have access to that or insurance providers have to have access to that information?" (F/BrC)
Negative implications or harms	"Yes, what are the possible ramifications, like everything? Like the question that I have now, like what haven't I thought of that could be a possible ramification of knowing? Yeah. So...speaking to a doctor about it would be great. Speaking to my doctor about what I could possibly learn that I might not want to know, that would be great." (F/BrC)
Theme 4: process of deliberation	
Deliberative decision-making process	"The only potential benefit I see is if it discovers something that could be dealt with and prevent serious illness or genetic problems in the future. So then, that would have to be weighed against the emotional and psychological effects. I guess it depends on the particulars." (M/CC)
Take time to decide	"I think I would want to think about it and talk about it a little more before I made that quick decision, yeah." (F/BrC)
Desire to consult others	"Well, I would probably discuss it with my wife. I think we're pretty much on the same page as far as the more information the better. It all depends on the information I guess. But I don't think it's something that we would shy away from." (M/LC)
Conduct independent research	"Well, I think I would research mutations first and find out a little about it before I answered him, but my nature is to go ahead and find out as much information as I can. So I would probably want him to do it. But, like I said, research it first." (F/BlC)
No need to engage in extensive deliberation	"I would say, 'Great, where do I sign?' When I first got diagnosed, I offered to have my DNA sequenced, and the doctor said, 'Why would you bother? There's only 30 markers, and we've already looked at them.' So yeah, to me, it was like a no-brainer and required no thought." (M/CC)
High value and utility of information	"Just my general feeling that more information is better. Information is power. I'd rather know than not know in most cases; in most cases...I value more information than less." (F/BrC)
Preference for quick decisions	"Minutes. I mean...for me, I'm generally a very fast decision maker. So for me, it's really once I understand what exactly I'll be getting out of the study or what benefit it can provide, that's enough of what I need to make a decision on. I wouldn't need to go back home and think about it." (M/CC)
Sense of urgency	"Oh, no, I'd definitely make a quick decision…because I'd want to seek treatment right away. I wouldn't want to procrastinate...it would be my decision....I'd discuss with family members...my husband and my sister, but...it would be my decision ultimately, and I'd really want to make it quickly." (F/BrC)

NOTE. The interviewer described secondary germline findings as follows: "I mentioned that with tumor genomic profiling, sometimes the lab will also look for mutations in the genes in your normal cells. Although the lab at 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." Participant characteristics are denoted after each quote as sex/cancer type.

Abbreviations: BlC, bladder cancer; BrC, breast cancer; CC, colorectal cancer; F, female; LC, lung cancer; M, male.

Theme 2: Vital Role of Doctors

Participants perceived their doctors (ie, oncologists) as a vital influence on their decision making. Several participants indicated that they would deeply value speaking with their doctor about the prospect of learning SGFs. The importance placed on this consultation and the doctor's personal opinion was partly a result of the *nature and quality of the doctor-patient relationship*. For example, several participants reported great trust in their doctors on the basis of a foundation of past experiences and certainty that their doctors will act in their best interests. Their decision to learn SGFs was contextualized

within an established, trusting relational dynamic; consequently, these participants indicated that they would be strongly inclined to learn SGFs if their doctor offered. Similarly, a few participants described how they generally feel comfortable with discussing important issues with their doctor. Doctors also were seen as experts who would serve as the *primary source of relevant and valuable information* necessary for the decision. Several participants anticipated that their doctors would possess expertise with regard to a range of issues relevant to SGFs and thus could help them to acquire all essential information.

Theme 3: Information Needs

Participants described a typology of information that they would require to make an educated decision about learning SGFs, including an explanation of whether SGFs would provide a *clinical benefit* to the patient, his or her family, or other cancer patients and whether these benefits would outweigh possible harms; *assistance in interpreting the meaning* of SGFs, such as the degree of certainty of the results and meaning of specific mutations; *degree of scientific uncertainty* of SGFs and confidence in their applicability to health decisions; description of the *testing procedure* in terms of the invasiveness of sample acquisition; information about *who will have access* to the findings (eg, insurers, health care providers); and *negative implications or harms* of learning SGFs for the patient and family, including unanticipated consequences. Many participants stated that they would ask questions about these issues to feel adequately informed, yet a minority doubted that they would have any specific questions if presented with this decision primarily because of placing a high innate value on SGFs.

Theme 4: Process of Deliberation

Two preferences emerged among participants with regard to the necessity to engage in an extensive decision-making process. A majority anticipated a *deliberative decision-making process* characterized by weighing potential benefits against harms to determine their interest in learning SGFs. (A detailed description of these perceived benefits and harms is provided elsewhere.[12]) Participants described procedural aspects of their deliberation and expressed a preference to *take time to decide*, during which they would consider the option on their own and seek out information about the value of SGFs. These participants also expressed a *desire to consult others* for their perspectives, including family, friends, and health care providers. Furthermore, a few participants expressed a preference to *conduct independent research* to learn more about receiving SGFs and the meaning of potential mutations.

A minority of the sample articulated *no need to engage in an extensive deliberation* to determine their interest in SGFs. These participants reported that there was virtually no decision to make because they were already certain of their interest. Several factors informed this perspective. First, these individuals perceived a *high value and utility of information*, including knowledge in general and knowledge related to their present or future health. Second, many expressed a characteristic *preference for quick decisions*; thus, they would immediately respond to a doctor's offer to learn SGFs without further contemplation. Finally, some described a *sense of urgency* about learning SGFs and stated the necessity to gain and act upon this information quickly to benefit their current health directly.

Preferences With Regard to Decision Scenarios

During the interview, participants were presented with challenging scenarios and asked to describe their preferences for how clinicians should handle these situations. Participants' opinions were quantified and are listed with illustrative quotes in Table 3. First, in response to the debate about the disclosure of SGFs,[26-29] we asked participants whether findings about diseases that have effective medical interventions or medication adverse effects (ie, actionable SGFs) should always be returned to patients. Most participants (28 [70%] of 40) stated that patients should be able to choose whether to receive this information, whereas a minority (12 [30%] of 40) stated that such information should always be disclosed to patients.

Participants also were asked to decide whether they believed that if actionable SGFs were detected after a patient's death, then these findings should be made available to a patient's family or significant other. The majority (36 [90%] of 40) reported that such information should be made available after a patient's death. This

perspective was motivated predominantly by perceived family health benefits. A subset of participants (16 [69.5%] of 23) also expressed a belief that patients should be required to provide consent for this disclosure before their death, such as at the time of agreeing to TGP, whereas fewer (seven [30.5%] of 23) deemed patient consent unnecessary. Only a few participants were

Table 3. Preferences With Regard to Specific Decision Scenarios That Involve Secondary Germline Findings and Illustrative Participant Quotes

Question	Participant Quote
Should actionable secondary germline findings* always be returned to patients?	
Yes (30%)	"Yes, I agree with that because they may not want to know, but they're still going to be affected by it. So I would...agree with that. Because at least they'd have the opportunity to know...what's going on with them. They may not want to know, and it may be painful, but I think that they should be told." (F/CC)
No (70%)	"Oh my goodness, that's hard. I don't know if I can answer that. I guess...yeah, there should be a choice because someone that might not be able to handle the information can choose to say, 'I don't want to know.'…I think [about] the burden of having a terminal illness and then finding out that there's more. I think of a very close friend that was diagnosed with cancer, and he was in his 20s, and he survived, but when I learned that I had cancer, I reached out to him, and he said that at his lowest point he begged, 'I don't want to know any more information. I can't handle it, just have my mom and dad.' And that was part of the healing for him, so I always think about that because that was a poignant point that he made, and I think it's so personal. So I think the person, the individual, should definitely have the choice. (F/BrC)
Should actionable secondary germline findings be made available to a patient's family or significant other if a patient has died?	
Yes (90%)	"Yes. Well, if it in any way could...impact the timing of treatment or care for someone else in the family, they should....I would want them to know about it....I guess at the end of the day that you should get consent from the patient...as to what you're going to do with anything...you take from them." (M/LC)
Unsure (5%)	"You got a coin; you wanna flip a coin? Because the problem that comes to me is that my family is very tight, and it wouldn't be a problem with my family, but you always have a family that [is]...on the outs, so to speak, and if you tell one, you got to tell all. So I guess it's all or nothing. It's not like you can pick and choose. I think the family has a—I don't want to use the word 'right' because I think they may need to know, to understand. But have the right? It's a toss-up. I guess it's situational." (M/LC)
No (5%)	"That's a good question because I'm thinking that if the spouse, for example, were told after the person passed away that we had discovered this, I guess the first reaction would be, 'How come we didn't discover it earlier while the person was still alive and there may have been time for some kind of treatment?' So it might cause some kind of anger. It might cause some kind of feeling that there was negligence on the part of doctors not to have discovered this or reveal it or whatever. So I don't know if that would necessarily be a good thing after a person passes away...unless there was a very strong reason to do that. But I would be cautious about that." (M/CC)
Should nonactionable secondary germline findings† be made available to a patient's family or significant other if a patient has died?	
Yes (82.5%)	"Yeah, I think it should be available. Well, just...helpful in identifying for them if they feel they should [have] mutation testing done to see if they also are carriers. I think they should be able to make that choice if it's been identified in one family member." (F/BlC)

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Table 3. Preferences With Regard to Specific Decision Scenarios That Involve Secondary Germline Findings and Illustrative Participant Quotes (Continued)

Question	Participant Quote
Unsure (2.5%)	"I can project how I might think in the future, but it's hard for me to say at this time in a practical way how I would feel about, you know, releasing." (F/LC)
No (15%)	"My gut reaction is no, and that's based on my personal experience. If they want the information they should go and get it...and I think that if they get it just because it was available for me, like as part of my estate, here's her genetic testing, and again, I'll use my brother because he has the kids. If...he sees in black and white that there's an indicator that we have a gene—I have a gene so that becomes a family gene--so he's now gotten a worry he didn't ask for in his life. You know, it's that gene. If I have a gene that could be terminal, not actionable... in today's world, like pancreatic cancer...which is...the worst cancer...in terms of how quickly it kills people that I know. I don't want him to know that." (F/CC)

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

Abbreviations: BlC, bladder cancer; BrC, breast cancer; CC, colorectal cancer; F, female; LC, lung cancer; M, male.

*In the interview, actionable secondary germline findings were described as follows: "There are different ways to think about the many kinds of mutations or disease risks that you could theoretically learn about. On the one hand, you could learn about conditions that have effective medical interventions. These could be conditions like some forms of cancer or conditions that put you at risk of heart disease or of having a heart attack. When doctors know that someone has one of these mutations, they can recommend ways to help prevent a disease from developing or help find it earlier when it is more likely to be treatable. The doctors may also change the kinds of medications that they prescribe."

†In the interview, nonactionable secondary germline findings were described as follows: "It is also possible that the lab will find mutations for conditions that do not have recommended or effective medical interventions. These could be common conditions like diabetes or incurable conditions like Alzheimer's disease. It is possible that learning about these mutations could motivate some people to change their lifestyle or make personal decisions about how they live their lives. The lab could also learn that you have a mutation that makes you a healthy carrier for a recessive disease such as sickle cell anemia or cystic fibrosis. Being a carrier has little or no effect on your health. But when two carriers of the same recessive mutation have a child, then the child could have the disease."

unsure about whether actionable SGFs should be available to a patient's family after death (two [5%] of 40) or stated that such information should not be made available (two [5%] of 40). Preferences against disclosure were due to concerns about negative emotional implications of such information for families.

Participants were similarly asked to decide whether they believed that SGFs about diseases without effective medical interventions or that indicate one is a healthy carrier for recessive diseases (ie, nonactionable SGFs) should be made available to a patient's family after a patient's death. Again, a majority stated that such information should be made available (33 [82.5%] of 40) largely because of the potential for family health benefits. Most participants who provided an opinion regarding consent reported that patients should be required to consent to the disclosure of this information to their families (11 [92%] of 12). Fewer (six [15%] of 40) stated that nonactionable SGFs should not be made available to family after a patient's death because of concerns about negative emotional reactions and the limited ability to intervene with such diseases. One participant (2.5%) was unsure. Finally, when comparing the preferences of participants with regard to the return of actionable versus nonactionable SGFs to family after a patient's death, 22.5% (nine of 40) were discordant in their preferences across these scenarios.

DISCUSSION

This study clarifies the decision-making processes of patients with advanced cancer with regard to SGFs from TGP. Given the personal nature of genetic risk information, participants viewed the decision to learn SGFs as ultimately their own. However, consistent with other medical decision contexts,[30-34] variability existed in participants' preferences for involving others, including spouses/partners, children, and siblings, in their decision making. Consequently, when presenting the option of learning SGFs, clinicians must allow patients to solicit input from close others and help to navigate challenges inherent in decision making with multiple individuals.[35] Additional research should investigate how such interpersonal influences shape, hinder, or support patients' SGFs decision making.

Participants anticipated that their doctors (ie, oncologists) would be the primary source of guidance for this decision. They placed great

trust in their oncologists and acknowledged the influence of their expertise and personal opinions on their decision making. Participants also anticipated that they would have extensive questions about the benefits, harms, interpretation, and process of obtaining SGFs and would expect their oncologists to provide answers. However, research has demonstrated that this may not be feasible because many oncologists have limited experience with germline testing and express concerns about their ability to address challenges presented by SGFs.[8] Several approaches may help to bridge this gap between patient expectations and oncologist preparedness, including oncologist-targeted communication training, novel patient education materials, and referral to genetic counselors to address patient questions. Future research should evaluate which of these approaches are most effective at achieving the delicate balance between meeting patients' information needs and practical challenges of cancer care delivery (eg, time demands, workforce limitations). Research should also examine how various models of patient education (eg, oncologist led, genetics professional led) influence patient SGFs decisions and how patients weigh the opinions of various care providers in this context.

Many participants anticipated a preference to undergo a thoughtful deliberation about the prospect of learning SGFs. Conversely, a minority believed that they would make an immediate decision guided by their personal values and beliefs. Research suggests that the adoption of a more intuitive decision-making approach can yield similar outcomes to deliberative decision making,[36] although both approaches have benefits and drawbacks.[37] Of note, some participants' preferences for a quick decision were motivated by beliefs that SGFs would provide clinical utility or necessitate urgent action for them to reap health benefits. These expectations may be inaccurate for many patients with advanced cancers because the information revealed will not change their prognosis or clinical management. Accordingly, clinicians must ensure that all patients, including those immediately enthusiastic or accepting of SGFs, accurately understand the limitations of this risk information.

These results also provide insight into preferences of patients with advanced cancers with regard to challenging scenarios that involve the return of SGFs. Consistent with American College of Medical Genetics and Genomics recommendations[4] and expert opinion,[38] most participants stated that patients should choose whether they want to receive actionable SGFs from TGP. Participants acknowledged that some individuals may not want this information and that clinicians should honor such preferences. In addition, participants expressed diverse opinions about the management of SGFs after a patient's death. Participants generally were more supportive of the return of actionable SGFs to family after a patient's death than nonactionable SGFs; although, in both instances, a majority supported the sharing of this information with family largely because of perceived family health benefits. The observation that 22.5% of participants held discordant views about the appropriateness of sharing actionable versus nonactionable SGFs with family after a patient's death highlights the importance of distinguishing the various categories of risk information that can be revealed through TGP[39] when educating patients and eliciting their preferences.[8,40] Participants' general approval of obtaining patient consent at the time of TGP to ensure preference-concordant management of SGFs after death reinforces current ethical recommendations.[41]

This study has notable strengths. The qualitative design enabled an in-depth analysis of the decision-making preferences of a sample of patients with advanced cancers diverse in diagnosis, sex, and health status. However, the majority was well-educated (85% reporting at least some college); decision-making preferences and processes of these individuals may differ from those with less formal education. Additional limitations are that this sample was racially and ethnically homogenous, recruited from one institution, and assessed at a time when the decision about learning SGFs was hypothetical in nature; thus, the findings may not be generalizable to the broader population of patients with advanced cancers treated in other care settings who are navigating this decision in real time. Future work should examine decision-making processes of more-diverse patients and evaluate how various approaches to presenting patients with the option of learning SGFs (eg, education and consent led by oncologists *v* genetics professionals, presentation during a medical oncology visit *v* a separate visit) ultimately influence patient decision making.

Table 4. Recommendations for Developing Precision Oncology Programs With Regard to How to Manage and Support Patient Decision Making About Secondary Germline Findings From Tumor Genomic Profiling

Develop educational materials about tumor genomic profiling (TGP) and secondary germline findings (SGFs) that can be easily disseminated to and understood by close others (eg, siblings, children, spouses/partners) who may play a role in a patient's decision making.
Ensure that individuals who lead education and consent discussions about the return of SGFs are prepared to help patients with varying preferences for decisional autonomy from their close others.
Patients attribute high trust and expertise to their oncologists; therefore, prepare oncologists to serve as a primary resource who can provide balanced advice to patients about SGF decisions.
Create patient educational materials that provide clear information about the potential benefits and harms of SGFs. Distinguish between potential outcomes of SGFs for patients (with a consideration of their cancer stage and prognosis) and their families.
Ensure that patients understand that the decision to undergo TGP is separate from the decision about return of SGFs and that varying potential benefits and harms of each choice exist.
Structure education and consent discussions about TGP and the return of SGFs to be temporally flexible and, therefore, capable of accommodating patients' preferences to take time to deliberate, seek additional input from close others, and conduct independent research.
Give patients a choice about the return of actionable SGFs. Either opt-in or opt-out models of germline variant management could allow such patient choice, but each has unique implications for resources to support informed patient decision making and subsequent uptake of SGFs.
Require patients to make decisions about the management of actionable and nonactionable SGFs in the event of their death at the time of consenting to TGP and the return of SGFs.

In conclusion, this study provides important insight into how patients with advanced cancers approach the decision to learn SGFs and informs how developing precision oncology programs can manage the reporting of germline variants from TGP (Table 4). A paternalistic model of care in which patients lack a choice about receiving SGFs is inconsistent with patient preferences. Precision oncology programs instead should establish models that empower patients to make informed decisions about whether to learn SGFs. Patient preferences for involvement in this decision can be accommodated in both opt-in and opt-out models, although these models likely will differ in the resources necessary to support patient deliberation and in the number of patients who select to receive SGFs.[42,43] Although most patients likely will want to retain decisional control in this context, some will desire time and space to include family and other influential figures in their decision making. Patients with advanced cancers likely have specific information needs, and possible misperceptions, about the implications and utility of SGFs. Oncologists will be the primary resource to which patients turn for clarity and guidance and must be prepared to meet these demands. Whereas the TGP decision may be time sensitive because of treatment implications, patients may benefit from efforts to ensure that the decision to receive SGFs can be pursued on a different temporal schedule that aligns with their preferences for information seeking and deliberation. Thus, educational and communication interventions targeted to patients, their families, and oncologists are needed to provide clear information that contextualizes the meaning of SGFs in the advanced cancer setting, assist the weighing of benefits and harms, and allow patients to explore and express their preferences about specific categories of SGFs and management of this information in the event of their death. Such interventions would enable the delivery of optimal decision support that matches patients' needs and preferences in this era of precision cancer care.

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