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Ovarian cancer patients' and their family members' perspectives on novel vaccine and virotherapy trials

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Abstract

Background/Aims—Some of the most promising avenues of cancer clinical investigation center on immunotherapeutic approaches. These approaches have provided notable gains in cancer therapeutics with recent FDA approvals of agents of this class in several types of cancer, although gains for ovarian cancer lag behind. This study examined perceptions of therapeutic trials including immunotherapy and virotherapy among ovarian cancer patients and their family members.

Methods—Seventy-two semi-structured qualitative interviews were conducted with 33 patients and 39 family members at two National Cancer Institute-designated comprehensive cancer centers. Eligible patients were diagnosed with epithelial ovarian, primary peritoneal, or fallopian tube carcinoma and had experience with clinical trial conversations; family members were nominated by patients and interviewed separately. Applied thematic analysis was used to understand and interpret the data.

Results—More participants were aware of vaccine trials than virus trials, although more than half had heard of at least one of them. Initial reactions to vaccine trials were generally favorable. For many, childhood experience with vaccines lent a familiar frame of reference. Virus trials elicited more negative initial reactions, including the use of adjectives such as “scary” and “dreadful.” Viruses seemed contagious or difficult to control. Increased receptivity to these trials occurred in the context of limited therapeutic options and cancer recurrence. Most participants,

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Declaration of conflicting interests

The authors have disclosed the federal funding sources of the work. The authors declare that there is no conflict of interest. The corresponding author had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

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including those not immediately drawn to these types of trials, indicated openness to learning more.

Conclusions—Although vaccine and viral trials are both immunologically-based therapeutic approaches, patients who are offered these trials may perceive their potential benefit and safety quite differently. There is a need to consider terminology, solicit and address “gut reactions,” and provide information that enables patients and their family members to better understand the science behind these trials.

Keywords

Ovarian cancer; clinical trials; qualitative; immunotherapy

Introduction

Clinical trials elucidate the efficacy and toxicity of drugs and drug combinations and ensure that cancer patients have a robust set of therapeutic options. Moreover, improvements in survival in certain cancer subgroups appear to be directly tied to greater participation in trials.¹ In this context, the fact that less than 5% of adult cancer patients enroll in clinical trials in the United States (US) is unfortunate, and impedes national agendas to advance cancer care.²

In ovarian cancer, the need to maximize clinical trial enrollment is immense. Ovarian cancer is the most lethal gynecologic malignancy, resulting in over 14,000 deaths annually in the US.³ Low trial accrual and all of its downstream consequences only punctuate the dearth of therapeutic options available to patients with this malignancy. Indeed, in the past two decades, only two new drugs have become available for the treatment of ovarian cancer; in contrast, several dozen drugs became available for other cancers, including 18 new drugs in 2015.⁴

Immunotherapy is defined as cancer treatment that attempts to incite the body's own immune system for antineoplastic purposes, i.e., to fight against cancer cells. In contrast, virotherapy uses viruses or components of viruses as either vectors to introduce antineoplastic agents into cancer cells or as direct anti-cancer, oncolytic agents. Immunotherapeutic approaches have provided notable gains in cancer therapeutics with recent approvals of agents of this class in several types of cancer, although gains for ovarian cancer lag behind.⁵ Furthering of these gains is contingent on adequate trial enrollment. A study by Minion and colleagues noted that 22% of respondents with ovarian cancer reported participation in a clinical trial.⁶ The authors noted the importance of including the voices of patients in clinical trial design in order to improve enrollment and enhance patient decision making. This point may be especially important for immunotherapy and virotherapy trials, which may be unfamiliar to many patients.

The objective of this research was to examine perceptions of immunotherapy and virotherapy trials among patients with ovarian cancer. Furthermore, we sought to understand the perspectives of family members, as these have been sparsely studied and may contribute to trial decision making.

Participants and methods

Eligible patients were adult women with a diagnosis of epithelial ovarian, primary peritoneal, or fallopian tube carcinoma (herein referred to as 'ovarian cancer') who had been offered a clinical trial opportunity (not limited to immunotherapy or virotherapy trials) at one of two comprehensive cancer centers in the Midwest. Each patient was asked to nominate one to four adult family members or close friends to participate in a separate interview. The Institutional Review Boards at Mayo Clinic (IRB# 12-007611) and University of Chicago (IRB# 13-0161) approved this research. All participants provided informed consent prior to being interviewed.

Individual interviews were conducted in-person or by telephone by experienced qualitative researchers (a PhD behavioral scientist and PhD and Master's trained qualitative analysts with expertise in family studies and health services research). Field notes were completed immediately following each interview to record any issues with the interview process and to begin reflection on the data. Audio files were transcribed and transcripts were reviewed by one or more investigators for accuracy. The use of a semi-structured guide provided standardization of key data while allowing the interviewer flexibility to elicit more detailed responses. Participants were asked to describe their initial reactions to vaccine and virus trials. Further questioning was aimed at uncovering trial-related attitudes that might influence enrollment decisions.

Information about clinical trial enrollment and disease characteristics including age and stage at diagnosis was abstracted from the electronic health record. Demographic characteristics of patients and family members including sex, age, race, ethnicity, education and employment status were collected via survey.

The study team regularly discussed their observations during concurrent data collection and analysis. At least two individuals independently coded each transcript and then met to discuss coding and come to agreement prior to entering data into NVivo software (NVivo 10.1, QSR International Pty Ltd.). Using methods of data analysis and interpretation similar to those described by Creswell,⁷ the investigative team categorized the coded data into themes and identified connections between themes. Written narratives and group discussion were used to find meaning in the data and summarize findings. Patient and family member interviews were analyzed separately to explore differences in perspectives; as differences were few, the findings are reported in aggregate. Data from the two institutions are similarly reported in aggregate.

Results

Thirty-three patients (27 from Mayo Clinic and 6 from University of Chicago) and 39 family members (35 from Mayo Clinic and 4 from University of Chicago) were interviewed. Family members included spouses/partners (n=13), adult children (n=8), siblings (n=6), parents (n=3), friends (n=6), and others (n=3). Fifty-seven interviews were conducted by telephone and 15 were completed in-person. Mean interview length was 48 minutes (range

20–77). Participant characteristics are shown in Table 1. Six patient participants enrolled in a vaccine trial and four enrolled in a virus trial before or during the study period.

The results of the qualitative analysis were categorized under two themes: “gut reactions” and “decision factors” as shown in Table 2 and described below.

Theme 1: “Gut reactions”

At least half of the participants had heard of vaccine or virus trials—more so vaccine trials than virus trials. Familiar or not, most participants expressed gut reactions to hearing them described; reactions were generally favorable and included comfort with the notion of vaccines as agents of prevention (for an illustration, see Quote 1, Table 2). Several participants talked about the historical development of vaccines, aiming to prevent disease rather than cure it, and changing the course of a disease (see Quote 2, Table 2). Some participants acknowledged negative perceptions of vaccines, including concerns about links between vaccines and autism (see Quote 3, Table 2), but most participants seemingly did not hold such perceptions. A negative gut reaction to a vaccine trial was expressed by one patient who recalled a news story about tainted shots administered in a US clinic. Another patient noted that in some vaccine studies, enrollment might require restricted contact with family members such as vulnerable adults or children.

Unlike vaccine trials, virus trials elicited more negative than positive gut reactions. Negative responses included “scary” and “dreadful.” Viruses seemed contagious or difficult to control; some participants expressed worry that the virus would mutate, spread, or cause damage. Unlike vaccines, a virus was something you would not want to come into contact with (see Quotes 4 and 5, Table 2). Participants had less understanding of how a virus could help with cancer, but they spoke about discoveries as being wonderful.

In contrast to those expressing immediate positive or negative reactions to vaccine and virus trials, some participants (particularly those who were not at all familiar with these trials) reacted with hesitation. Importantly, almost no reactions to either type of trial completely closed the door, but some participants wanted to know more before sharing their impressions.

Theme 2: “Decision factors”

Participants talked about information needs differently for vaccine and virus trials. Most participants said they would want similar information for a vaccine trial as they would for any other type of clinical trial, such as information on side effects. Some participants expressed awareness of mild side effects from vaccines, such as redness at the injection site. Others asked about allergies to eggs or other vaccine-related allergies. Some participants voiced a fear that some aspects of therapy might be unknown, but the unknowns of vaccines appeared balanced by the potential for good, including fewer or different side effects and longer duration of benefit than the chemotherapies patients had received previously.

In contrast, many participants were intrigued but largely unfamiliar with virus trials and wanted to know more, including whether the virus was live, how prior childhood vaccines would impact effectiveness, and whether the virus was contagious. Participants surmised that

side effects -- especially long-term side effects -- were unknown, which elicited fear. And viruses seemed risky.

Some participants seemed to hold virus trials to a higher “certainty standard” than vaccine trials, potentially because of the greater likelihood of harm (see Quote 6, Table 2). If a vaccine did not work, it did not work; but if a virus trial was ineffective, it could potentially cause harm. Several participants presumed virus trials would be safe by the time they were enrolling cancer patients at comprehensive cancer centers.

Twenty-three patients had recurrent cancer or were experiencing cancer progression at the time of their interview, including the four patients who consented to a virus trial. Negative reactions to these trials were mediated by context. Patients expressed being more receptive if their therapeutic options were limited, using terms like “last resort.” Some participants in remission at the time of the interview expressed reluctance to be in a vaccine trial while things were going well, while others saw vaccine trial participation as a way to “do something” rather than wait for the cancer to return. Paradoxically, some highly receptive patients were ineligible for vaccine trials based on their disease stage (see Quotes 7–9, Table 2).

Discussion

Some of the most novel and promising avenues of clinical investigation involve immunotherapeutic approaches.^{5,8–11} Focusing on patients with ovarian cancer, an insidious disease with a poor prognosis and high recurrence rate for which only two new drugs have become available in the past 20 years, captures the perspectives and motivations of cancer patients for whom early-phase clinical trial availability and enrollment are critical.

One salient finding of this study is the charged effect of terminology that may be unique to immunotherapy trials. In reality, vaccine and viral trials have tremendous overlap; both are immunologically-based in their mode of action. Yet in many cases, participants voiced very different initial reactions to these trials. Many individuals relied on a familiar frame of reference from childhood and perceived vaccines as more benign, prevention-oriented, and perhaps safer than a viral-based trial. Such differences in perception underscore the need to adjust terminology in trial conversations to minimize the effect of potentially strong negative gut reactions to virotherapy. Our data suggest however that even in the face of negative reactions, individuals are receptive to information about these trials. Information should focus on the scientific rationale behind immunotherapy and span the different types of trial conversations outlined by Wall et al.¹² to “prime” cancer patients and their families to make well-informed decisions about participation.

Another important finding of this study dealt with the long journey traversed by many ovarian cancer patients by the time they were offered a trial. Consistent with a report by Cohen et al.¹³ addressing quality of life among Phase I trial participants, patients in this study seemed motivated to enroll in trials that might have fewer side effects or at least a different side effect profile from previously received cancer therapy. In this context, a novel approach seemed welcome not only because it might be effective but also because it might

be more tolerable. This latter point is perhaps not considered as carefully in trial conversations as the purported anticancer effects of a novel therapy.

This is the first study to qualitatively depict gut reactions (positive and negative) to using vaccines and viruses to fight cancer. Immunotherapy trial discussions may benefit from conversations that carefully elicit initial reactions from patients and family members, including prior experiences with vaccines and viruses. In particular, terminology surrounding the use of viruses may evoke negative reactions that impede the ability to fully engage individuals in trial conversations. Expressions of hope, fear, or doubt can be used as a starting point for explaining the science behind the safety and promise of vaccines and viruses and fully engaging patients and family members in a discussion about immunotherapy trials.

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Table 1Participant characteristics (*n*=72)

Characteristic	Patient <i>n</i> =33	Family Member <i>n</i> =39
	<i>n</i> (%)	<i>n</i> (%)
Female	33 (100)	23 (59)
Employment Status		
Employed full-time or part-time	14 (42)	21 (54)
Not working for pay	19 (58)	16 (41)
Missing	0	2 (5)
Educational Attainment		
Some high school or diploma/GED	9 (27)	1 (3)
Some college or associate's degree	6 (18)	13 (33)
Bachelor's degree or higher	18 (55)	23 (59)
Missing	0	2 (5)
Race		
White	31 (94)	37 (95)
Other (Mexican)	1 (3)	0
Other (Puerto Rican)	1 (3)	0
Missing	0	2 (5)
Hispanic Ethnicity		
Yes	2 (6)	0
No	31 (94)	37 (95)
Missing	0	2 (5)
Age at interview, in years		
Mean $\pm$ SD (range)	59 $\pm$ 9.9 (36–76)	56 $\pm$ 13.4 (25–81)

GED, graduate equivalency degree; SD, standard deviation.

Table 2

Qualitative themes and representative quotes

Theme	
Gut Reactions	1. <i>"When I was still a little kid and I wasn't even 7–8 years old, I got the polio vaccine and it was like a miracle drug. ... vaccine, it is a very positive word for me."</i> [14A - patient]
	2. <i>"But to find a vaccine for it, just made so much more sense to me, just like with smallpox or other diseases, that you don't necessarily have to cure them but you can give them a vaccine to prevent it..."</i> [12A - patient]
	3. <i>"I was vaccinated for whooping cough... But I had a friend who chose not to do her children because she was worried about autism and all of that. Her daughter got whooping cough and I saw what that did."</i> [105A - patient]
	4. <i>"Viruses just kind of scare me....they are that thing that you can't touch. Nothing touches it, you know, nothing can help you when you have a virus....and then you always hear of, like if a virus starts it goes into your blood stream or it can go into your brain...it could make something worse happen."</i> [21A - patient]
	5. <i>"Live virus has loaded definitions. And when you say vaccine it seems a little more benign. A live virus...seems a little less benign."</i> [16B – adult child]
Decision Factors	6. <i>"Your immune system is really compromised, now you are going to introduce something that will possibly give you the measles...now, that could be fatal at that point. You know, somebody would have to convince me that that might be a good idea, something that is going to work."</i> [3B - spouse]
	7. <i>"Yah, that was – we were very eager to hear about (the vaccine trial), and also after hearing about it, to participate in it...It is something that provides additional hope for us. ...Um, it is sort of a reinforcer that we are doing something additional than not doing anything."</i> [21B -spouse]
	8. <i>"I really wanted to be on that (vaccine trial) and...it hasn't worked yet and I guess there are so many on the waiting list anyway. But you have to be in remission and that is really hard for me to do. I get about 6–8 months of remission every year and a half or so. The stars would have to align but I would totally be up for that... It's that pesky remission thing. It never works out properly."</i> [13A - patient]
	9. <i>"Well...because of the high probability of her cancer returning it was something that definitely – I mean it is just like thinking about getting a vaccine for the chicken pox, you know. You want to try it because you don't want to have to worry about what is going to happen if they do come back."</i> [17B - spouse]