Patients' Perceptions on Participation in a Cancer Chemoprevention Trial

Joseph A. Tangrea,[1] Maria Elena Adrianza, and William E. Helsel

Cancer Prevention Studies Branch, Division of Cancer Prevention and Control, National Cancer Institute, NIH, Bethesda, Maryland 20892 [J. A. T.], and Information Management Services, Inc., Silver Spring, Maryland 20904 [M. E. A., W. E. H.]

Abstract

The perceptions of patients regarding the benefits, disadvantages, and importance of their participation in a long-term cancer chemoprevention trial, the Isotretinoin–Basal Cell Carcinoma Prevention Trial, were assessed through a questionnaire mailed at the conclusion of the 3-year treatment period of the trial. Responses were evaluated overall, as well as within subgroups defined by sex, age, education level, treatment group, presence of side effects, and the number of skin biopsies performed during the 3-year intervention phase. Overall, "careful medical follow-up received" (43%) and "being part of a research effort" (24%) were the most frequently cited important benefits, while the "amount of time taken to attend clinic" (32%) and "side effects" (20%) were the most frequently cited unpleasant aspects of trial participation. Most surveyed patients viewed the study as "very or extremely important" to their general health (62%) and their skin cancer condition (88%) and, as a result of participation, felt "much or somewhat better" physically (52%). The majority indicated that they would "definitely or probably" be willing to take part in another research study (79%) and take the study medication, if it were shown to be effective in the trial (78%). Overall and subgroup data provide important insights into patient motivations and attitudes regarding cancer chemoprevention trial participation, adherence, and satisfaction.

Introduction

Published information on patients' attitudes about participating in clinical trials is limited. Although reports on participants' opinions on taking part in epidemiological research have appeared in the literature (1–4), limited systematic research has been done regarding the perceptions of patients enrolled in long-term, large-scale clinical trials. Of the few published studies providing direct information on attitudes toward clinical trials (5–10), only one surveyed patients who were actually participating in a clinical trial (7). In that study, Mattson *et al.* (7) ascertained the opinions of participants in two long-term multicenter clinical trials sponsored by the National Heart, Lung and Blood Institute. Information on perceived benefits, satisfaction, and disadvantages of participating in the trials was obtained by interview or questionnaire shortly before each trial was unblinded and the patients informed of the study outcome. Altruistic motivations were evident in both trial populations. Additional medical monitoring, opportunity for a "second opinion," and reassurance were cited most frequently as advantages of participation, while clinic waiting time and transportation problems were perceived as the main disadvantages.

In contrast to cancer treatment, cancer chemoprevention is targeted at reducing cancer incidence and usually involves the long-term administration of specific chemically defined agents, such as vitamins or their synthetic analogues, in patients at risk of developing primary or secondary cancers (11). Due to the chronic nature of the interventions in chemoprevention research, long-term adherence of trial participants to both the intervention and the protocol is a major issue (12). To better design and administer cancer chemoprevention trials, it is important to have insight into the attitudes and perceptions of potential trial participants. In this report, we present data on the benefits, disadvantages, importance, and satisfaction perceived by patients enrolled in a double-blind, placebo-controlled, multicenter chemoprevention trial examining the efficacy of a synthetic retinoid in preventing the new occurrence of BCC.[2]

Materials and Methods

The Clinical Trial. The ISO-BCC Study was a double-blind, randomized, placebo-controlled clinical trial designed to evaluate the effectiveness of the oral intake of low-dosage levels (10 mg/day) of a synthetic retinoid, isotretinoin, in reducing the incidence of basal cell carcinoma in a population at high risk of developing these skin tumors and to examine the possible side effects associated with the long-term administration of low doses of isotretinoin (13). The accrual phase of the study, during which 981 patients were enrolled, started in February 1984 and closed in June 1987. Overall, one of five patients contacted, either through clinic visit, questionnaire, or telephone, was ultimately enrolled in the trial at eight clinical centers in the United States. To be eligible to participate in the trial, a patient had to be a white male or female between the ages of 40 and 75; had to have had two or more biopsy-proven BCCs during the 5 years before randomization; have normal liver and renal

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[1] To whom requests for reprints should be addressed.

[2] The abbreviations used are: BCC, basal cell carcinoma; ISO-BCC Study, Isotretinoin-Basal Cell Carcinoma Prevention Trial.

function; had to have given written, informed consent; be willing and able to participate for the duration of the trial; have the entire skin surface evaluable for presence of BCC; had to agree not to take high-dose vitamin A (>5,000 units/day); and, for women, be incapable of childbearing. After meeting these eligibility criteria and giving written informed consent to participate, patients were randomized to take either 10 mg of isotretinoin or a matching placebo daily for 3 years. Once randomized, study participants were scheduled to report for follow-up clinic visits at 2 weeks, 3 months, 6 months, and every 6 months thereafter for 3 years of intervention and up to 2 years postintervention.

The trial found no difference in the cumulative incidence of the first new BCC between the isotretinoin and placebo groups and no reduction in the multiplicity of BCC, as measured by tumor rate (14). In addition, we observed that the number of patients who experienced elevated total serum triglycerides and mucocutaneous reactions was significantly higher in the isotretinoin group compared to patients in the placebo group (14). The overall percentage of patients with adverse reactions in the isotretinoin group was 76%. However, 43% of the patients in the placebo group also experienced "adverse" reactions, primarily symptoms related to skin and mucous membrane drying (mucocutaneous) or muscular aches and pains (arthralgia/myalgia). Most adverse reactions reported in both the isotretinoin and placebo groups were mild in nature, and dose modification was considered necessary for less than 20% of the reactions (14).

The Patient Survey. A survey was developed as a questionnaire and mailed to all trial participants still being followed as they completed the 3 years of intervention with isotretinoin or placebo. The main areas addressed by the questionnaire included the perceptions of patients regarding:

- benefits of study participation;
- unpleasant aspects of study participation;
- importance of study participation to general health and skin cancer condition;
- physical well-being;
- willingness to take active treatment if shown effective;
- participation in future trials

All questions were close-ended, requiring the participant to choose one of a number of given responses. Only if an "other" benefit or disadvantage was perceived were participants asked to specify by using an open-ended format. Batches of questionnaires were mailed at monthly intervals between July 1989 and October 1990. Completed surveys were returned within 1 month of receipt. Nonrespondents were mailed a second questionnaire with a cover letter. An overall response rate of 97% (864 of 891 patients surveyed) was obtained.

Data Analysis. In order to exclude potential bias, only those patients who completed the questionnaire before notification of their treatment group assignment are included in the analyses (n = 793). To determine whether baseline demographic characteristics (age, sex, education) or factors related to intervention and/or protocol (treatment group, presence of side effects, and number of skin biopsies performed) modified perceptions on trial participation, responses to each question were stratified by baseline covariate and evaluated using a χ^2 statistic (15).

Table 1 Group characteristics of survey respondents

	Total (n = 793) n (%)
Demographic characteristics	
Sex	
Male	614 (77)
Female	179 (23)
Age	
<63 years	394 (50)
63+ years	399 (50)
Education	
High school or lower	300 (38)
College or higher	493 (62)
Intervention-related characteristics	
Treatment group	
Isotretinoin	396 (50)
Placebo	397 (50)
Presence of side effects	
Yes	473 (60)
No	320 (40)
Number of skin biopsies	
0–6	394 (50)
7+	399 (50)

Results

The characteristics of survey respondents (n = 793) are shown in Table 1. Subgroups defined by sex were balanced by education level, treatment group, and side effects, but differed in age and in the number of biopsies undergone (mean age: men, 61.8 years; women, 59.9 years; mean number of biopsies: men, 10.2; women, 5.8). The isotretinoin and placebo groups differed only in the percentage experiencing side effects (isotretinoin group, 76%; placebo group, 43%). All other subgroups were balanced with respect to each of the other covariates. These characteristics were not different from those of the overall ISO-BCC Study population (data not shown).

Overall survey results are presented in Table 2. Survey responses stratified by baseline demographic characteristics and intervention-related characteristics are presented in Tables 3 and 4. On average, for each question, 3% of patients either did not respond (left answer blank) or provided multiple responses. These data were included in the bivariate subgroup analysis of responses but are not shown in Tables 3 and 4.

What is the most important benefit received from study participation? Of the 793 patients in this sample, the most frequently cited important benefit of participation (Table 2) was the "careful medical follow-up received" (43%). The next most frequent responses were "being part of a research effort" (24%) and the "potential for reducing skin cancer" (17%).

In the analyses of subgroups defined by baseline demographic characteristics, we found that responses to this question differed significantly by sex and education

Table 2 Overall survey responses

	(*n* = 793) *n* (%)
Q.1. Most important benefit from study participation	
Careful medical follow-up	340 (43)
Part of a research effort	191 (24)
Potential for reducing skin cancer	138 (17)
Overall improvement in patient care	44 (6)
Other	13 (2)
Q.2. Most unpleasant aspect of study participation	
Amount of time taken to attend clinic	252 (32)
Side effects from study medication	160 (20)
Number of blood samples taken	83 (11)
Chance of taking isotretinoin or placebo	66 (8)
Need to take capsules every day	60 (8)
Additional medical procedures undergone	40 (5)
Number of questions asked at each visit	16 (2)
Other	29 (4)
Q.3. How important is study participation to your general health?	
Very/extremely important	495 (62)
Fairly important	178 (22)
Not/slightly important	110 (14)
Q.4. How important is study participation to your skin cancer condition?	
Very/extremely important	700 (88)
Fairly important	51 (6)
Not/slightly important	20 (3)
Q.5. As a result of study participation, how do you feel physically?	
Much/somewhat better	412 (52)
No difference	340 (43)
Somewhat/much worse	21 (3)
Q.6. If isotretinoin is shown effective, would you take continuously?	
Definitely/probably	617 (78)
It depends	108 (14)
Probably/definitely not	51 (6)
Q.7. If asked, would you take part in another research study?	
Definitely/probably	625 (79)
It depends	128 (16)
Probably/definitely not	34 (4)

[a] Blank or multiple responses to each question not shown.

(Table 3). "Careful medical follow-up" was reported more frequently by patients with a college or higher education. In contrast, those who cited "being part of a research effort" were more frequently women and those with a high school education or less.

None of the intervention-related factors (Table 4) influenced responses to this question.

What is the most unpleasant aspect of study participation? The "amount of time it took to attend clinic" was the most frequently cited unpleasant aspect of study participation (32%) (Table 2). The next most frequently cited unpleasant aspects were the "side effects from the study medication" (20%) and the "number of blood samples taken" as part of the protocol (11%).

Sex was the only demographic factor that influenced the response to this question, with the largest differences seen in the proportions of men and women responding with "amount of time it took to attend clinic," "side effects from the study medication," and "additional medical procedures undergone" (Table 3).

We also observed significant differences between certain subgroups defined by intervention-related factors, *i.e.*, treatment group and side effects (Table 4). While respondents in the placebo group regarded the "amount of time it took to attend clinic" as the most unpleasant aspect of study participation more frequently, a greater proportion of patients in the isotretinoin group than in the placebo group viewed the "side effects from the study medication" as the most unpleasant aspect. "Side effects" was listed by a greater percentage of patients who actually experienced side effects during the intervention period, compared to those who did not experience these.

How important is ISO-BCC Study participation to your general health? Most surveyed patients (62%) viewed the study as very or extremely important to their general health (Table 2).

Responses to this question differed only by age and level of education (Table 3). Older patients and patients with a high school education or less indicated more frequently that study participation was "very or extremely important" to their general health. Patients who stated that the study was "fairly important" tended to be younger respondents and in the higher education group. Patients with a college or higher education responded that the study was "not or slightly important" to their general health more frequently than those in the lower education group.

How important is study participation to your skin cancer condition? Overall, an overwhelming majority of respondents (88%) felt their study participation to be "very or extremely" important to their skin cancer condition (Table 2). We found no significant differences among subgroups in response to this question.

As a result of study participation, how do you feel physically? Slightly more than one-half of all surveyed patients (52%) felt "much or somewhat" better physically as a result of their participation (Table 2).

A greater proportion of men responded that they felt "much or somewhat" better. The majority of the women surveyed reported feeling "no difference" (Table 3).

Patients in the placebo group reported feeling "no difference" more frequently than those in the isotretinoin group. Although few patients overall stated that they felt "somewhat or much worse" (21 patients of 793 surveyed), those in the isotretinoin group, as well as those with more skin biopsies, were more likely to give this response (Table 4).

If isotretinoin is shown to be effective, would you take continuously? Most patients (78%) indicated that they would "probably or definitely" be willing to take isotretinoin continuously if it was found to be effective in preventing skin cancer (Table 2).

Among baseline demographic characteristics, only sex influenced the response to this question. A much larger proportion of men, compared to women, expressed a willingness to take the study medication continuously, if it were shown to be effective. Of those who were more hesitant, a larger percentage were women (Table 3).

In the analyses of subgroups defined by intervention-related factors, patients in the placebo group and those who did not experience side effects responded affirmatively more often. Patients who indicated that they would "probably or definitely" *not* take the study medi-

Table 3 Survey responses by baseline demographic subgroups

Question/response[a]	Sex		Age		Education	
	Male (n = 614) %	Female (n = 179) %	<63 years (n = 394) %	63+ years (n = 399) %	High school or lower (n = 300) %	College or higher (n = 493) %
Q.1. Most important benefit from study participation						
Careful medical follow-up	44	38	43	43	35	47
Part of a research effort	22	32	22	26	31	20
Potential for reducing skin cancer	16	21	19	16	19	17
Overall improvement in patient care	6	3	5	7	5	
Other	2		2	2	2	
p[b]	0.003		NS		0.005	
Q.2. Most unpleasant aspect of study participation						
Amount of time taken to attend clinic	35	21	31	32	34	30
Side effects from study medication	18	28	20	21	19	21
Number of blood samples taken	10	13	12	9	10	11
Chance of taking isotretinoin or placebo	9	4	8	9	9	8
Need to take capsules every day	8	7	9	6	6	
Additional medical procedures undergone	4	10	6	5	7	4
Number of questions asked at each visit	2	3	1	3	2	2
Other	4	1	5	3	2	
			NS		NS	
Q.3. How important is study participation to your general health?						
Very/extremely important	64	59	57	68	73	56
Fairly important	23	21	26	19	18	25
Not/slightly important	13	18	16	12	8	17
p	NS		0.009		<0.001	
Q.4. How important is study participation to your skin cancer condition?						
Very/extremely important	88	89	89	88	92	86
Fairly important	7	6	8	5	4	8
Not/slightly important	2	3	3	3	2	3
p	NS		NS		NS	
Q.5. As a result of study participation, how do you feel physically?						
Much/somewhat better	55	42	51	53	53	51
No difference	40	53	44	41	40	45
Somewhat/much worse	2	3	3	2	4	2
p	0.008		NS		NS	
Q.6. If isotretinoin is shown effective, would you take continuously?						
Definitely/probably	81	68	80	75	76	79
It depends	12	21	13	14	16	12
Probably/definitely not	6	8	6	7	6	7
p	0.002		NS		NS	
Q.7. If asked, would you take part in another research study?						
Definitely/probably	81	71	79	78	76	80
It depends	14	23	17	16	20	14
Probably/definitely not	4	6	3	6	3	5
p	0.007		NS		NS	

[a] Blank or multiple responses to each question not shown.
[b] From χ^2 statistic. NS, nonsignificant.

cation continuously, even if it were shown to be effective, were more likely to be those in the isotretinoin group or those who experienced side effects (Table 4).

Would you take part in another research study? Overall, the majority (79%) indicated that they would "definitely or probably" be willing to take part in another research study, while only a few said they "probably or definitely" would not (Table 2). Of the subgroups, sex was the only factor which significantly influenced patients' responses to this question. A larger percentage of men indicated that they would "definitely/probably" take part in another study. Women appeared more hesitant than men regarding this question, with 23% indicating that "it depends," compared to 14% of men.

Discussion

The present study differs from others (5, 6, 8–10) in that the patients surveyed were actual participants in a clinical trial, and thus, their opinions were based on their own experience and not on hypothetical trial participation or situations.

It is important to note that factors related to the nature of the ISO-BCC Study and the characteristics of the trial population could have affected patients' perceptions and attitudes regarding their participation in the trial. Trial participants were at high risk for developing new basal cell carcinomas, a form of skin cancer requiring routine surgical removal and regular follow-up to detect and treat new lesions. The study protocol was designed

Table 4 Survey responses by intervention-related subgroups

Question/response[a]	Treatment group		Side effects		Number of skin biopsies	
	Isotretinoin (n = 396) %	Placebo (n = 397) %	Yes (n = 473) %	No (n = 320) %	0–6 (n = 393) %	7+ (n = 400) %
Q.1. Most important benefit from study participation						
Careful medical follow-up	45	41	45	40	39	47
Part of a research effort	23	25	22	27	25	23
Potential for reducing skin cancer	17	18	16	19	20	15
Overall improvement in patient care	6	6	6	5	7	5
Other	2	2	2	2	2	2
P[b]	NS		NS		NS	
Q.2. Most unpleasant aspect of study participation						
Amount of time taken to attend clinic	27	37	30	34	30	34
Side effects from study medication	28	12	24	15	22	18
Number of blood samples taken	11	10	11	9	12	9
Chance of taking isotretinoin or placebo	7	10	9	8	6	10
Need to take capsules every day	7	8	6	10	8	7
Additional medical procedures undergone	4	6	5	6	5	
Number of questions asked at each visit	1	3	1	3	3	1
Other	4	4	3	4	3	5
	<0.001		0.010		NS	
Q.3. How important is study participation to your general health?						
Very/extremely important	65	60	64	59	61	64
Fairly important	21	24	22	23	23	22
Not/slightly important	13	15	13	16	14	14
P	NS		NS		NS	
Q.4. How important is study participation to your skin cancer condition?						
Very/extremely important	89	88	89	87	89	88
Fairly important	6	7	6	8	7	6
Not/slightly important	3	3	3	3	3	2
P	NS		NS		NS	
Q.5. As a result of study participation, how do you feel physically?						
Much/somewhat better	53	51	51	53	51	53
No difference	39	47	42	44	46	40
Somewhat/much worse	4	1	3	3	1	4
P	0.001		NS		0.005	
Q.6. If isotretinoin is shown effective, would you take continuously?						
Definitely/probably	72	83	74	83	77	79
It depends	17	11	15	12	15	
Probably/definitely not	9	4	9	3	6	
P	0.003		0.005		NS	
Q.7. If asked, would you take part in another research study?						
Definitely/probably	78	80	77	82	81	77
It depends	17	16	18	14	16	17
Probably/definitely not	4	4	5	3	4	
P	NS		NS		NS	

[a] Blank or multiple responses to each question not shown.
[b] From χ^2 statistic. NS, nonsignificant.

to maintain the same pattern of follow-up visits, thereby not changing the patients' routine care. In addition, many participants already had an established relationship with their clinical center dermatologist, who served as a trial investigator, further contributing to improved compliance.

Our finding that careful medical follow-up received was the most frequently cited benefit from study participation parallels responses given through other surveys by both actual participants in clinical trials (7) as well as patients and members of the general public considering future participation (9). The time it took to attend the clinic (which included clinic waiting time and transportation problems) was also the most frequently cited unpleasant aspect in both this and the study conducted by Mattson *et al.* (7).

We found some interesting differences in perceptions between subgroups of respondents, particularly those defined by sex, level of education, treatment group, and experience of side effects. In our study, men and women clearly had different views as to what they considered beneficial, unpleasant, and important about trial participation. They also differed in their expressed willingness to participate in another trial, with women showing a lesser willingness. This is somewhat paradoxical, given the greater altruism expressed by women, and suggests that the perception of unpleasant aspects may have been a more important determining factor in this decision for women. Our findings contrast with those of Mettlin *et al.* (6), who reported no significant sex differences in the expressed interest to participate in cancer prevention research among potential study participants.

With recent emphasis on the underrepresentation of women as subjects in clinical research, an understanding of sex differences as they relate to motivation, satisfaction, and participation in clinical trials is both timely and important.

By education level, we also observed a difference in how patients viewed the benefits of study participation, with greater altruistic motivation expressed by those survey respondents with fewer years of formal education (high school or less). The perception of well-being and importance of the trial to a patient's general health also differed by his/her educational level.

Except for the more frequent perception among older patients that study participation was very important to their health, the absence of significant differences in responses by age group is noteworthy.

Differences observed among demographically defined subgroups, in particular those by sex and education, can be consequential to patient recruitment and adherence. As Cassileth *et al.* (9) point out, the less common motivations and perceptions of patients are often underemphasized in the recruitment process. Including these in discussions with potential trial participants may well optimize the recruitment process and attract a more heterogeneous population.

The process of recruiting patients to participate in clinical trials is highly selective. The representativeness of these trial participants to those of the overall population of skin cancer patients is an important issue. The perceptions of our trial participants were, as shown, influenced by factors specific to the design of the trial, the intervention, and the nature of the disease under study. However, rather than diminishing the value of the results, this emphasizes the importance of thoughtful study design and quality administration in maintaining patient interest and satisfaction while taking part in long-term clinical trials.

Consideration of these findings in conjunction with other related studies can provide meaningful insights necessary to attract potential participants not currently represented in clinical trials. Once patients are enrolled in a trial, awareness of their motivations and perceptions regarding participation can be useful in improving both compliance and satisfaction.

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