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The Quest for Treatment: Cancer Patients' Experience of Phase I Clinical Trials

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Nursing

by

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ABSTRACT OF THE DISSERTATION

The Quest for Treatment:
Cancer Patients' Experience of Phase I Clinical Trials

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Phase I clinical trials of new anticancer drugs and therapies, while critical to the development of new treatment, rarely benefit participants directly. Despite the potential risks and unknown benefits, however, many patients willingly enter these trials. Researchers know little about their motivation for doing so or the effect of their participation on their quality of life. The purpose of this study was to explore and describe, from the perspective of the patient, the essential structure of the lived experience of participating in Phase I clinical trials.

This study used a phenomenological approach, assuming that the way to understand a phenomenon of interest is through the subjective words of the person who has experienced it.

Tape-recorded unstructured interviews were used to elicit participants' verbal descriptions of their experience. After informed consent was obtained, the Folstein Mini-Mental State examination was administered to screen out participants with cognitive impairment. Participants who passed the examination were interviewed. Whenever possible, the participants were interviewed twice: once soon after they are enrolled in a clinical trial, and once several weeks later.

Phenomenological analysis of the data revealed common categories and themes, which were then summarized and integrated into a consistent description of the meaning of the experience. The overall theme that emerged from the interviews was the Quest for Treatment. This theme captured the experience of most participants, who described being diagnosed with cancer, exhausting standard treatment and then beginning a quest for additional treatment, including clinical trials. The Quest for Treatment was seen as an active process that follows a typical course, marked by steps along the way. These steps emerged as categories across the narratives: (a) Taking Charge, (b) Deciding, (c) Living on a Trial, and (d) Dealing with Uncertainty. Although these categories are consistent with other recent studies of the perceptions of cancer patients on clinical trials, the overall theme of a quest for treatment has not previously been identified.

Chapter 1: Introduction

Developing new anticancer drugs and therapies is critical in the war on cancer. Since the organization of the Cancer Chemotherapy National Service Center in 1955, more than 370,000 substances have been evaluated for antitumor activity (Gross, 1986). These substances must, of course, be tested on human volunteers and must show benefit before they can be approved for general use. Clinical trials serve as "the bridge between the basic research laboratory and the patient's bedside" (Jenkins & Curt, 1991, p. 355).

Objective tumor response and increased survival are the traditional markers of benefit from new therapies. In recent years, however, the United States Food and Drug Administration (FDA) has made explicit its concern with quality of life in the testing of new anticancer drugs (Johnson & Temple, 1985). Benefit to quality of life is now one of the two requirements for approval of these new drugs, the other being improved survival. Indeed, a new agent can be approved if it improves quality of life alone, whether or not it also increases survival (Cella, 1992).

This explicit interest in quality of life in clinical trials is related, in part, to increasing survival rates for cancer patients, and in part to a growing awareness on the part of the FDA and health care providers that patient benefits from treatment are not related solely to survival

rates (Padilla et al., 1983). According to Redmond (1997), "The primary endpoints measured in trials today relate to a drug's antitumour effect...but these endpoints are limited in that they give no information about the effect of the treatment on the person with cancer" (p. S11).

In spite of a growing awareness that benefits to patients may depend on other factors such as quality of life, the lack of both clearly defined concepts and of standard measures have inhibited the use of such indicators (Ferrans, 1990; Redmond, 1997; Simon, 1989). Thus, there is still a need to determine from patients themselves just what benefits derive from treatment and how treatment affects their quality of life. This study focused on the experience of cancer patients undergoing Phase I clinical trials from the perspective of the patient.

Clinical Trials

The testing of new therapies for cancer proceeds through several stages. National Cancer Institute (NCI) computers scan the structures of roughly 40,000 newly synthesized chemicals each year. Approximately ten of these compounds will eventually be tested in human subjects (Jenkins & Curt, 1991).

Of the new compounds screened, computer analyses select approximately 10,000 compounds that show unique structures, probable anticancer activity, and a rational biochemical design. These agents are then tested against

human tumor cells grown in culture (Jenkins & Curt, 1991). Federal law also requires that the agents be thoroughly tested for toxicity in animals before being given to humans (Jenkins, 1996).

Preclinical testing thus establishes the pharmacology of a drug and its efficacy in tumor systems in vitro or in animal models. Preclinical testing also gives information about expected toxicities. Following preclinical testing, investigators begin testing promising agents in Phase I, II, and III trials. Phase I trials represent the first test of a compound in humans, using a small number of patients treated at escalating dose levels. Because, in the interest of patient safety, the initial doses are usually below the therapeutic range, direct benefit to the patient in these studies is rare (Simon, 1997). In fact, in a review of 228 Phase I trials, only 6% of patients achieved an objective tumor response (Von Hoff & Turner, 1991). Earlier investigators found only a 4.3% response rate (Estey et al., 1986).

Phase I clinical trials are designed to determine the relationship between toxicity and the dose-schedule of treatment (Jenkins, 1996). Additionally, researchers collect data on absorption, blood levels achieved, and the metabolism and elimination of the drug by the body (Jenkins & Curt, 1991). Because of the significant risks involved in these first trials, eligible patients are those who have

no other therapeutic options. Often, these are patients who are terminally ill (Arvay, 1991). Because there is no necessity for demonstrating therapeutic benefit in Phase I clinical trials, the only valid reason for not proceeding to the next stage of testing, Phase II trials, is the determination of unacceptable toxicity in the drug (Jenkins, 1996).

After toxicity data have been established in Phase I trials, Phase II trials determine the drug's effectiveness against specific tumor types (Jenkins, 1996). Patients eligible for these trials are again those who have not benefitted from standard treatment or for whom no standard treatment is effective. In addition, they must have measurable tumors so that tumor response can be determined (Jenkins & Curt, 1991). Phase II trials test those tumor types that have shown some promise of responding in Phase I trials (Grant & Padilla, 1990).

Phase III clinical trials then compare those agents that demonstrate efficacy in specific tumor types in Phase II trials with standard therapy. In these studies, patients who have had no prior treatment are randomly assigned to receive either the investigational treatment or standard therapy (Jenkins & Curt, 1991). Phase III trials require large numbers of subjects and long periods of follow-up in order to establish the superiority of one treatment over another in terms of survival, disease-free

survival, and quality of life (Hubbard, 1982; Jenkins, 1996).

Finally, after testing lasting approximately 14 years and costing as much as 50-70 million dollars, a new agent may become commercially available (Gross, 1986). However, prior to wide-spread commercial distribution, researchers may conduct additional studies, known as Phase IV clinical trials, to determine the optimal use of the new agent within existing treatment regimens (Jenkins & Curt, 1991).

Because clinical trials involve the use of human experimental subjects, they are subject to extensive government regulation. The Department of Health and Human Services (DHHS) and the FDA have established criteria to be followed in designing a clinical trial. These criteria include: a good research design, competent investigators, a favorable balance of risks and benefits, an informed consent process, and the equitable selection of subjects. All trials conducted at a given institution must also be reviewed by an institutional review board in order to assure the protection of the human subjects involved (Jenkins, 1996).

Risks and Benefits of Phase I Clinical Trials

Many of the regulations involved in clinical trials are designed to ensure that the risk of harm to the subjects does not exceed the possible benefits to those same subjects or to future patients. The decision as to

when the possible benefits outweigh the risks involved is a critical but challenging one. As one nurse scholar pointed out:

> At issue in deciding benefit is who should make the decision whether an innovative treatment is beneficial enough to undergo risks. Does the patient or research subject make this decision? Or is benefit decided by the researcher or those caring for patient subjects? (Fry, 1989, p. 1035).

Direct benefit to subjects of clinical trials as well as future benefits to patients from the development of new therapies are the benefits at issue. While there has been speculation that subjects derive benefit from participating in clinical trials (Bernheim, 1987; Grant & Padilla, 1990; Kodish, Lantos, & Siegler, 1990), few investigators have explored patients' actual lived experience in these trials.

Significance of the Problem

It was through my own practice as an oncology nurse that I first became concerned with understanding the experience of patients on clinical trials. It has been my observation that, despite careful informed consent procedures, patients have varied perceptions of the purpose, risks, and benefits of the trials in which they participate. They remember little of the information given in the course of obtaining informed consent (Larson &

McGuire, 1990) and often seem not to be concerned with specifics. It occurred to me that the information we present to patients may not be personally relevant to them. A more appropriate way to inform patients may be to present information related to the experience of participating in the trials rather than simply the facts associated with them. My clinical observations suggest that this experience may be meaningful to patients in different ways.

One patient I cared for, for example, an ex-Marine, seemed particularly eager to participate in the research. When asked why, this man expressed his desire to contribute to the care of future patients. He demonstrated less concern with the progression of his own disease than with the hope that we might "learn something" from his experience. During the course of his investigational treatment, this patient was hospitalized for many weeks. He had no visitors other than his wife and a young priest with whom he had established a relationship. Although he died in treatment, the nursing staff was able to reassure him before his death that we had, indeed, learned much from him. His ability to make that contribution seemed to give meaning to the end of his life.

Another patient, a young man with osteogenic sarcoma, revealed that he personally had no wish to participate in the clinical trial in which he was enrolled. However, he explained that his parents and his physician had staked

everything on this last investigational effort to get his disease under control. Therefore, although he had no anticipation of personal benefit, he agreed to participate in order to please the important persons in his life. This patient completed the trial but died of his disease.

In working with these and other patients on clinical trials, I began to suspect that personal benefit may not be the most important consideration for some patients who enroll in clinical trials. Hope and altruism, for example, may both play a role in their participation.

However, the state of knowledge about the personal experience of patients undergoing clinical trials is extremely limited. Clinicians probably don't fully understand why patients elect to participate in clinical trials and what impact their participation has on their lives. Because of the lack of quality of life data on these patients, investigators conducting clinical trials have had to make certain assumptions regarding the risks and benefits involved in them (Bernheim, 1987). However, if patients are to make informed choices about the appropriateness of a clinical trial for themselves, and if nurses and other clinicians are to provide care and support to these patients, specific knowledge is essential.

Campbell (1976) has suggested that "the quality of life lies in the experience of life" (p. 118). Not knowing what the experience of clinical trials is like for patients

places researchers and clinical staff in a precarious position. How can they facilitate the decision process and provide ongoing care to patients who elect to participate if they do not understand the experience? Without research studies on which to base our understanding, we cannot make assumptions about that experience with any degree of confidence.

Having available information about the lived experience of participating in Phase I clinical trials has ethical implications not just for a particular clinical trial but for all Phase I clinical trials. Such information may validate the assumptions of benefit commonly cited by investigators. If, as Yoder and associates (1997) have found, these benefits are not realized by the patients, then what benefits do accompany study participation? Are there none? In that case, we need to revise the risk-benefit ratio commonly ascribed to clinical trials. We can no longer balance the individual's risks against personal benefits but must weigh the known risks to the individual against the benefit to future patients. If, however, there are benefits to participation in clinical trials, as clinical experience and the available data seem to suggest, then it is important to know the nature and scope of such benefits. Clinicians could present such information to patients during the decision making process and also use it to select patients

for accrual into clinical trials. Again, if specific quality of life data were available, the nurse would have a better opportunity to provide appropriate support to patients on clinical trials.

Perhaps the benefit is hope. Nurses can intervene to increase and maintain hope both in patients on clinical trials and in patients on standard treatment or supportive care (Hickey, 1986; Koopmeiners et al., 1997; Poncar, 1994). Perhaps the benefit is the fulfillment of altruistic motives. In that case, nurses could increase the benefit by providing feedback on the importance of the trial and on the preliminary findings. Perhaps patients are motivated primarily by the desire to please family and health care workers. In that case, nurses would have significant information on the patients' sources of social support.

Thus, it is critical to know the impact of clinical trials in general on patients' lives. Whatever the actual benefits and risks of participating in clinical trials, both the investigator and the clinical staff need to be aware of them. It is clearly unethical to recruit patients to participate in clinical trials without providing them as much information as possible about what impact participation will have on them. That information must be based on scientific evidence rather than guesswork.

In addition, it is important to know the effects on

quality of life of specific clinical trials. Knowing the answers to such questions as "How does this investigational treatment affect the patient's quality of life?" and "Does the treatment increase or decrease life satisfaction?" in addition to other outcome information could contribute to the evaluation of new drugs and the planning of optimal therapy for each individual with cancer (Schipper & Levitt, 1985; Speca, Robinson, Goodey, & Frizzell, 1994).

Finally, it is my conviction that patients rely heavily on their professional caregivers for information and support during the course of treatment. We are failing our patients if we cannot respond appropriately to them by providing specific information and supportive care tailored to their individual needs. Only by understanding what their participation in our studies is likely to mean to them, can we provide this care.

Purpose of the Study

The purpose of this study was to explore and describe, from the perspective of the patient, the essential structure of the lived experience of participating in Phase I clinical trials. That is, the study sought to identify the meaning of the experience for patients and the ways in which their participation affected their lives.

Because researchers know so little about the actual experience of these patients, a qualitative design can best address the research question. Phenomenology is the most

appropriate approach for this task as it seeks to describe and understand human experience from the perspective of those who live it (Oiler, 1982). Phenomenological exploration is the crucial first step in identifying the specific elements along with the range of variables associated with patients' experience on clinical trials.

One of the objectives of this study was to clearly define constructs that have been applied to cancer patients' experience but which have remained vague in the literature. One of these constructs is "quality of life." As will be shown, quality of life may encompass a broad range of variables and may, in fact, be impossible to compare across studies because of the lack of consistent operational definitions (Ferrans, 1990) and because it may actually have different meanings for different patients (Cella, 1994).

Another construct that may relate to the experience of cancer is "meaning in life." Trice (1990) defined meaningful experience for elderly persons through phenomenological methods, but meaning in life has not yet been clearly defined for cancer patients. Only qualitative research methods can provide the data necessary to achieve an understanding of "meaning" in the lives of cancer patients.

Finally, some researchers have identified altruism as a factor in patients' participation in clinical trials

(Mattson, Curb, McArdle, & the AMIS and BHAT Research Groups, 1985). My own clinical experience tends to validate these findings. But what is altruism? How do patients view their motives? What does it mean to say that an activity is motivated by altruism? It is hoped that these and other constructs may be clarified by appealing to the source: the patients' own perceptions of their experience as they have lived it.

Lynch-Sauer (1985) has suggested that "nursing, as a science, has a goal to understand those individuals being cared for in order to know how to care for them" (pp. 105-106). Nurses caring for patients undergoing clinical trials need to understand those patients' expectations and experiences in order to provide care to them when their expectations are not met as well as when they are. This study, by identifying benefits that patients receive from their participation as well as their perceptions of risk, may provide clues to the later development of specific interventions that nurses can use to strengthen the informed consent process and to provide support to patients on clinical trials. Specifically, interventions that enhance hope and quality of life may be relevant. Additionally, a knowledge of patients' experiences may suggest ways to facilitate recruitment of appropriate patients into trials.

With clinical trials now being conducted not only in

designated cancer centers but also in community hospitals under the administration of cooperative study groups, more and more nurses in the community will need to be familiar with these trials and what they are likely to mean to their patients. This study could provide some direction in educating nurses in those insights and in specific interventions as suggested above.

This phenomenological exploration was a crucial first step in identifying some of the factors that influence patients' participation in clinical trials as well as their quality of life while participating. The findings obtained suggest further research. For example, researchers might undertake studies to confirm results across demographic and illness categories. Ultimately, those variables that appear to be important in determining patients' responses to clinical trials could be measured using either existing or newly developed scales.

Phenomenological inquiry is a process of theory generation (M. J. Smith, 1989). As such, it differs from quantitative work which is used to test theories. This study resulted in a thorough description of the experience of actual patients participating in clinical trials. Findings from this study could potentially contribute to the development of a theory constructed on this description that is faithful to the reality experienced by patients in Phase I clinical trials and is therefore particularly

relevant to nursing's knowledge of human responses to health phenomena.

This study investigated the experience of participating in Phase I cancer trials from the viewpoint of the participant. The design and findings of the study are described in the following chapters. Specifically, the following chapters will provide: (a) a review of relevant literature to date, (b) an explanation of the organizing framework for the study, (c) a report of the study design, (d) a description of the researcher as instrument, (e) an overview of the major findings of the study, (f) a summary of the major themes identified, and (g) a discussion of the limitations and implications of the study findings.

Chapter 2: Review of the Literature

Few studies delineate cancer patients' experience with clinical trials. Consequently, this review of literature focuses on existing related research that explores presumed influences on cancer patients' perspective or experience: (a) cancer patients' perceptions of quality of life, (b) patients' decision making, coping, and perception of benefit from clinical trials, and (c) cancer patients' attempt to maintain hope and find meaning in their experience.

Quality of Life

While researchers conducting clinical trials regard quality of life as a relevant and important concern, its assessment has been hampered by a lack of conceptual clarity. In order to develop tools that accurately and reproducibly measure quality of life, it is necessary to define the concept (Ferrans, 1990). Although researchers do not agree on the definition of quality of life or on health-related quality of life, certain defining characteristics can be established.

Most researchers view quality of life as a multidimensional construct (Aaronson, 1986; Calman, 1987; Cella, 1994). The dimensions measured vary by the instrument and the investigator, but may include the following domains: physical, functional, psychological, social, sexual, and spiritual. According to Cella, these

multiple domains can be grouped into four primary dimensions: physical, functional, emotional, and social. As Ferrans (1990) has pointed out, even when multiple dimensions are assessed, it is necessary to establish the importance each domain has for the individual in order to get a clear picture of its impact on quality of life. In this study, quality of life is assumed to be multidimensional with individual variation.

Additionally, researchers conceptualize quality of life as subjective (Aaronson et al., 1991; Calman, 1987; Cella, 1994; Ferrans, 1990). Although a few scales of physical functioning are used to estimate quality of life, estimates made by observers have not been shown to correlate highly with patients' own determinations of their quality of life (Cella & Tulsky, 1991; Slevin, Plant, Lynch, Drinkwater, & Gregory, 1988).

Recent investigators have made a case for proxy ratings of quality of life in the case of patients with advanced disease (Brunelli et al., 1998; Sneeuw et al., 1997). Sneeuw and colleagues found substantial agreement between patients with brain cancer and their significant others. They recorded agreement if the two responses were within one category of one another. However, since the majority of questions in their quality of life scales contained only four response categories, a difference of one category might significantly change a response (from

"somewhat" to "not at all," for example). Also, Slevin et al. (1988) pointed out that simple correlation between responses may not adequately measure agreement. They reported, "Even with a seemingly 'good' correlation coefficient of, say, 0.7 only 50% of the variability in one set of scores is explained by the other. Thus differences between scales can be easily overlooked" (p. 110). For this reason, it is necessary to ask the patient directly about his/her quality of life.

Quality of life cannot be intuitively determined. In a classic study of patients with sarcomas, Sugarbaker, Barofsky, Rosenberg, and Gianola (1982) found that limb-sparing surgery did not always result in a higher quality of life than amputation when measured by patient report. Because of the unforeseen adverse effects of the radiation therapy used in the limb-sparing protocol, many patients reported greater interference with their quality of life, especially in the areas of sexual and functional abilities (Sugarbaker et al.). Using these results has enabled oncologists to modify the treatment regimen to reduce the impact on quality of life (Barofsky, 1986).

In addition to being subjective, quality of life is assumed to be dynamic (Calman, 1987; Cella, 1994). Perceived quality of life can vary with the person's circumstances, and health-related quality of life is certainly affected by the individual's health status.

However, the external circumstances of patients do not wholly determine their perceived quality of life (Speca et al., 1994). Also suggested to be important in establishing quality of life are expectation, uncertainty, and personality factors such as hardiness and optimism (Campbell, 1976; Padilla & Grant, 1985). Cohen, Mount, Tomas, and Mount (1996) found the existential domain to be an important determinant of quality of life, especially for patients with advanced disease.

One definition of quality of life includes the attribute of appraisal. Kleinpell (1991), in her concept analysis, identified two essential attributes of quality of life, one of which is "an evaluation, appraisal, or assessment of life" (p. 224). Similarly, Barofsky (1986) discussed quality of life assessment as a judgment process engaged in by an individual. He contrasted this approach with the psychosocial approach which he feels is more concerned with individual coping than with understanding differences in assessed quality of life. Again, Sartorius (1987) and Cella (1994) both used the definition of quality of life as an appraisal of one's life with regard to happiness, satisfaction, and the accomplishment of desired goals. For this study, health-related quality of life is defined as the subjective appraisal, from the perspective of the individual, of the meaning and satisfaction of life in response to changes in health status.

In addition to the increased interest in quality of life as it relates to cancer treatment, a few studies have used quality of life data to specifically assess the impact of clinical trials on the lives of cancer patients. The classic study by Karnofsky, Abelmann, Craver, and Burchenal (1948) on the use of nitrogen mustard for palliation of carcinoma used both tumor response and performance status to evaluate the effect of treatment. In more recent years, a number of clinical trials have employed quality of life instruments (Ganz, 1990; Bernhard et al., 1998).

In one such study, Coates et al. (1987) examined the quality of life of two groups of patients receiving chemotherapy for advanced breast cancer. One group received continuous chemotherapy according to a standard protocol while the other group received chemotherapy for a short time and then, in an effort to minimize side effects from the drugs, was given a rest until disease progression was evident (Coates et al.). The authors hoped that the intermittent chemotherapy would result in an improved quality of life as measured by a linear analogue scale with patients serving as their own controls. Instead, they obtained the opposite results. Not only did the intermittent therapy group have a significantly inferior tumor response to treatment, but they also reported deterioration in physical well-being, mood and appetite, and overall quality of life (Coates et al.). This study

demonstrates the importance of quality of life data in comparing two treatment regimens. It also demonstrates the need to evaluate treatment options that include "active supportive care" (Stjernsward, Stanley, & Koroltchouk, 1986).

In clinical trials, quality of life data, in addition to being useful in evaluating different treatments, may also have implications for patient selection. As Bernheim (1987) has argued, "the major ethical problem involving quality of life resides in phase I trials" (p. 15). Since these trials rarely result in objective benefit for the patient, investigators make certain assumptions. These may include the following: that the patient benefits medically from increased interactions with the physician, that there is a chance of objective improvement for the patient, and that there is a psychological benefit from participation in the trial per se (Bernheim). Because almost no studies have been done of the respective quality of life of patients treated in such trials and those treated less aggressively, these assumptions cannot be verified. Quality of life data on patients who participate in clinical trials, then, would provide valuable information on the consequences of therapeutic options. This information could guide physicians and nurses involved in patient accrual to trials and could impact the patient's decision on whether or not to participate (Bernheim, 1987;

Redmond, 1997).

Patient Perceptions of Clinical Trials

To date, researchers have made few attempts to study the quality of life of patients on Phase I trials. Berdel and associates (1988) found no significant differences in performance status or quality of life, as measured by a self-assessment scale, between patients on Phase I trials and patients receiving standard treatment. These results support those of Melink, Von Hoff, Clark, and Coltman (1985), who found no significant differences in quality of life between patients on clinical trials and those who had similar disease stages but were ineligible for the studies due to comorbid disease.

However, the linear analogue self-assessment (LASA) scale (Priestman & Baum, 1976) used by these investigators to measure quality of life relies heavily on reports of symptom distress and may not correlate well with psychosocial measures. In fact, Meyerowitz, Sparks, and Spears (1979) interviewed breast cancer patients on adjuvant chemotherapy and found that "the overall level of distress experienced by the patients did not relate significantly to the physical side effects of treatment" (p. 1617). Therefore, it is important to examine the experience of these patients from a psychosocial perspective as well.

Yoder, O'Rourke, Etnyre, Spears, and Brown (1997)

examined some of the assumptions of benefit referred to above. They interviewed 37 patients enrolled in Phase I clinical trials and found that patients expected their participation to result in a decrease in their tumor along with their symptoms, a decrease in hospitalization, an increase in communication with their physician, an increase in family support, and an increase in activity level. Most patients did not realize these expectations but still reported "no regrets" over their decision to participate (Yoder et al.). Clearly, then, other factors were operating. These factors have not yet been identified nor addressed but may be related primarily to quality of life.

Another study that specifically explored patients' perceptions of a clinical trial in which they participated found that most patients had a positive attitude toward the trial and that 78% stated that they would participate again, if asked. The most frequently cited benefits included additional medical monitoring, the opportunity for a second opinion, and reassurance (Mattson et al., 1985).

This study also found a high incidence of altruistic motives among participants. In fact, the investigators found that 65% of patients surveyed in the Aspirin Myocardial Infarction Study (AMIS) reported altruistic motivations for participating (Mattson et al., 1985). Since "altruism" was not operationally defined, however, one can only infer from their discussion of the findings

that it refers to "helping others." Similarly, the participants in the Beta-Blocker Heart Attack Trial (BHAT) are reported to have perceived about equal benefits to self and others (Mattson et al., 1985). The inference, then, is that benefits to "Scientists," "BHAT staff," "Other heart patients," "Family members," and "Friends," as determined by the questionnaire, represent "altruism." This lack of an adequate definition is especially frustrating in that the high degree of altruism found in their study was not evident in previously published studies (for example, Barofsky and Sugarbaker (1979), who found that participants acted primarily out of self interest).

Llewellyn-Thomas, McGreal, Thiel, Fine, and Erlichman (1991) conducted another study dealing with patients' perceptions of benefits from clinical trials. In this study, the investigators designed instruments to measure patients' attitudes towards decision control and benefits in a hypothetical clinical trial. Those who would refuse to participate in the trial sought more participation in decision making and demanded a greater benefit-to-risk ratio than those who agreed.

Although these studies differed considerably in design, both dealt with some aspect of patients' perceived benefits in participating in clinical trials. Mattson and associates (1985) also identified a perceived benefit to others (altruism), and Llewellyn-Thomas et al. (1991)

postulated that preference for participating in treatment decision making was associated with willingness to participate in clinical trials.

Taken together, these two studies paint quite different pictures of patients participating in clinical trials. Llewellyn-Thomas' (1991) group found patients to be generally reluctant to participate and to be motivated predominantly by their perception of benefit to themselves, at least in a hypothetical situation. In the Mattson et al. (1985) study, on the other hand, patients generally held favorable opinions of clinical trials and were motivated almost equally by self-interest and altruism.

Several differences between these studies may account for these different findings. First, the Llewellyn-Thomas (1991) study used a hypothetical situation presented to cancer patients to determine preferences while Mattson and associates (1985) queried heart patients already participating in trials. Both the disease and the sample variables may be significant in accounting for the difference. In addition, the self-report data may reflect a different attitude from that expressed in the tasks designed by Llewellyn-Thomas et al. (1991).

Clearly, further research needs to be done in this area. It is important, for example, to study patients who actually have to decide whether to participate in clinical trials rather than those who are deciding on a hypothetical

situation. In addition, constructs such as altruism need to be clarified in terms of the patient's own experience.

Rodenhuis and others (1984) of the Netherlands conducted interviews with participants in Phase I clinical trials for the purpose of evaluating the quality of an informed consent procedure and assessing their motivation to participate. They found the patients "motivated by hope for improvement of their conditions, pressure exerted by relatives and friends, the desire to contribute to the progress of medicine or simply because they felt they had 'no choice'" (p. 457). Although of the ten patients interviewed, two were unable to recall that their treatment was experimental, the authors concluded that the informed consent procedure was satisfactory and that written informed consent was not necessary. They also noted, however, that "many of the adequately informed patients have in fact a quite different perception of their position than one should expect on the basis of the information recalled" (p. 461). They pointed out that unrealistic expectations persisted in spite of clear statements that the effect on the tumor would be uncertain.

This study also asked the question, "Does the patient feel that the treatment adds to the quality of life or would -in retrospect - refusal to participate have been a better choice?" (Rodenhuis et al., 1984, p. 458). However, the only answer given to that question was that "no patient

spontaneously expressed regret at having participated" (p. 460) despite the fact that only two patients believed that the treatment was effective. This finding was echoed by that of Yoder and others (1997) thirteen years later and leaves open the question of what the benefit to these patients was.

Two more recent studies have looked at perceptions of patients who participate in Phase I trials, one in the United States and one in England. Daugherty and others (1995) at the University of Chicago conducted structured interviews with 27 patients who had recently signed informed consent for a Phase I trial and concluded that "cancer patients who participate in phase I trials are strongly motivated by the hope of therapeutic benefit. Altruistic feelings appear to have a limited and inconsequential role in motivating patients to participate in these trials" (p. 1062). These authors also noted that the participants felt that they had an adequate knowledge of the risks involved but did not recognize that the purpose of the trial was not therapeutic.

Another study conducted in England with seven patients on clinical trials (though only one was on a Phase I trial) found that they were motivated by "hope, a desire to help others, they felt they had no other choice, the wish to take part in research, and family pressure" (Cox & Avis, 1996). These participants were followed throughout the

trial and generally described themselves as having little choice but to participate in the trial and as leaving the overall decision about their treatment up to their doctor. The authors conclude with the suggestion that "the concepts of choice and hope and what they actually mean within these early anticancer drug trials warrants further consideration and exploration" (p. 184).

Stetz (1993) reported on a grounded theory study of the experience of patients and their spouses on experimental treatment for cancer, although not specifically a Phase I trial. This study identified "survival work," which was described as "the work of cognitively and behaviorally choosing life over death" (p. 122). Themes related to survival work included engaging, monitoring, and carrying on. Quality of life issues were not specifically addressed.

Of these studies, only the one by Stetz specifically addressed the experience of the patients themselves, although she was also concerned with spouses and health care professionals. In her grounded theory study, participants were undergoing an investigational procedure (chemoembolization) for the treatment of liver cancer but were not involved in Phase I trials.

Patient Control of Decision Making

The desire for control over decision making with regard to treatment options may be a factor in patients'

consent to participate in clinical trials. Several studies have examined cancer patients' desire for control over treatment in general and have related that desire to such variables as information-seeking (Brockopp, Hayko, Davenport, & Winscott, 1989; Cassileth, Zipkis, Sutton-Smith, & March, 1990). Information-seeking, however, has not always been found to correlate positively with the desire for participation in decision making (Sutherland, Llewellyn-Thomas, Lockwood, Tritchler, & Till, 1989). For example, Hack, Degner, and Dyck (1994) found that patients desiring active involvement in treatment decision making also desired illness- and treatment-related information, while some passive patients desired minimal information. However, they also identified some passive patients who wanted detailed information. Therefore, they found no simple relationship between the desire for control in treatment decisions and the desire for information.

In the area of clinical trials, two studies have recently examined patients' desire for control over treatment in relation to participation in clinical trials. Llewellyn-Thomas and associates (1991) found that patients who sought more participation in decision making regarding treatment were more likely to refuse to participate in hypothetical clinical trials. Dudjak, Wesmiller, and Sekula (1992), on the other hand, in interviewing patients who had already chosen to participate in clinical trials,

found the desire for control over one's choices was a significant factor in patients' decisions to take part in the study. Again, it is apparent that hypothetical situations are not always congruent with the actual situation that a cancer patient faces.

Outcome framing may also have an impact on patient's decision-making about treatment. That is, whether treatment information is presented by health professionals in a positive or negative light may influence patients' decisions (Hughes, 1993). To date, researchers have reached no consensus about this suggested effect, however. McNeil et al. (1982) found that outcome framing had an impact on treatment decisions, with more patients selecting a particular treatment when the problem was framed in terms of the probability of living rather than the probability of dying. However, a similar study using breast cancer patients selecting adjuvant treatment found no significant difference in the number of patients choosing nonstandard treatment, including clinical trials, when negative outcome framing (in terms of the risk of recurrence) rather than positive outcome framing (in terms of survival or cure) was used (Siminoff & Fetting, 1989). Again, in a more recent study, Hughes (1993) found no differences related to outcome framing in patient choices for breast cancer treatment. Thus, the role of patients' preference for participation in decision making in the selection of

clinical trials has not been established.

One perspective on patient decision-making was given by Kelly-Powell (1997), who used a grounded-theory approach to study the way heart, kidney, and cancer patients made treatment decisions. She found that, in accepting or rejecting treatment, patients relied more heavily on their perceptions of its effect on their lives than on estimations of its effectiveness. She referred to this decision-making process as "personalizing choices" (p. 221). These findings may account for some of the differences observed in the studies of outcome framing, above.

Coping

Baltrusch and Waltz (1987) have suggested that quality of life is related to coping. According to this model, the diagnosis of cancer affects quality of life by increasing negative emotions and by limiting opportunities for positive experiences. The coping activities of cancer patients are aimed at reducing negative affects and maintaining sources of personal gratification and "daily uplifts" (Baltrusch & Waltz, 1987). Accordingly, measures of coping, body image, self-esteem, mood states, and social adaptation were found to correlate with quality of life. Whether coping is related to clinical trial participation has not been investigated, however.

Herth (1989) found a relationship between hope and

coping in patients undergoing chemotherapy. Patients with the highest level of hope as measured on the Herth Hope Scale also had the largest number of coping responses. Rustøen (1993) suggested that hope is a strategy for coping and quality of life the result of successful coping. Poncar (1994) also suggested that, "having hope and being able to cope well are essentially the same" (p. 35). In this way, hope, coping, and quality of life may be related.

Hope and Meaning

Hope is an important concept in working with patients with life-threatening diseases such as cancer. It has been suggested that hope is related to the success of treatment as well as the patient's quality of life (Good, Good, Schaffer, & Lind, 1990; Rustøen, 1993; Whall, 1989).

Parallels may also be drawn between the concepts of quality of life and hope. Whereas quality of life involves an appraisal of the extent to which an individual has attained desired goals, hope is the expectation of attaining such goals in the future (Dufault & Martocchio, 1985). In addition, many of the empirical referents of hope are relevant to quality of life. These include making plans for the future, taking action to improve one's health, seeking and maintaining interpersonal relationships, and demonstrating positive affect as well as problem-focused coping responses (Mack, 1992).

O'Connor, Wicker, and Germino (1990) looked at hope

within the context of cancer patients' search for meaning in their lives. They defined hope as "the expectation of achieving a future good which seemed realistically possible and was personally significant" (p. 173). Sources of hope identified included cancer treatment and caregivers. Ballard, Green, McCaa, and Logsdon (1997) also found that patients drew hope from healthcare professionals and their treatments. Thus, clinical trials could promote hope in patients by providing continuing treatment.

A more recent study (Taylor, 1993) found that patients who adjusted well to their recurrent cancer (as measured by the Psychosocial Adjustment to Illness Scale) also demonstrated a clear sense of meaning on the Purpose in Life (PIL) Scale. Taylor also found an inverse relationship between sense of meaning and symptom distress and noted that middle-aged, married adults, as a group, had the highest PIL test scores. However, in her commentary on Taylor's work, Coward (1993) points out that meaning in life is a complex concept that may not best be measured by paper-and-pencil tests. As suggested by Wolfer's (1993) article on ways of knowing in nursing, Coward proposes a more appropriate qualitative design to emphasize the context of each person's experience.

There may be a relationship between the need for meaning in life and the desire to help others. Trice (1990) conducted a phenomenological study of the meaning of

life for elderly persons. She found that in order to experience life as meaningful, the elderly needed to feel "needed by, helpful to or useful to another person or group" (Trice, 1990, p. 251). If the same relationship holds true for cancer patients on clinical trials, the desire to help others may account for the altruism identified by some investigators (Mattson et al., 1985; Yoder et al., 1997) which may, in turn, enhance quality of life.

This review of literature has examined current knowledge of possible influences on cancer patients' experience of participating in Phase I clinical trials, including quality of life, decision making, coping, and meaning. No study has recently explored patients' experience and the meaning that they ascribe to it. This investigation, by interviewing the patients themselves, sought to identify the central characteristics of the experience of participating in Phase I clinical trials.

Chapter 3: Organizing Framework

Because this study was concerned with the actual lived experience of the patient from the patient's perspective, a phenomenological approach was chosen. Phenomenology, as a philosophical movement, originated with Edmund Husserl, who built on the work of Franz Brentano. Husserl's work was later expanded and refined by a number of his followers (Cohen, 1987; Spiegelberg, 1982). Husserl envisioned phenomenology as a means of enabling science to define and describe its foundations (Spiegelberg). He believed that the natural sciences and psychology had deteriorated into collections of facts with no real understanding of the phenomena with which they were concerned. Therefore, he declared the necessity of returning "to the things themselves" in order to clearly define human experience (Kohák, 1978). By beginning with the "things," that is, with phenomena, Husserl hoped to develop a science firmly rooted in an understanding of human experience. Later, other phenomenologists continued this tradition, including Martin Heidegger, who introduced an emphasis on interpretation, and Maurice Merleau-Ponty, who studied human perception from the perspective of the individual's experience (Cohen; Spiegelberg).

The phenomenological approach, as described by Husserl, is associated with phenomenological rather than positivistic assumptions about reality. For example, while

the natural sciences assume that an objective world exists independent of the observer and that it is possible to study it, phenomenology asserts that individuals can only know the world through the subjectivity of being in the world. That is, although we frequently think of the world as being divided into objective and subjective realities, we actually know the world only as we experience it, only as we, through our consciousness, act upon it and interact with it (Omery & Mack, 1995).

Based on these assumptions, then, it does not make sense to separate reality into "subjective" mind and "objective" world; there is only the lived experience of reality (Kohák, 1978). To say that something is real is to say that it is part of experience, but not that it is necessarily a physical entity. Whether our experience involves direct sensory perception of objects and people, memory, imagination, or dreaming, our experience is our reality (Kohák). In fact, we use such phrases as "it wasn't real to me" and "only x was real to me." "Real to me," in this case, means, quite literally, real (Omery & Mack, 1995).

Since the reality of a phenomenon cannot be known apart from a person's experience and interpretation of it (M. C. Smith, 1989), what science needs to explain, then, is not objects but experiences (Kohák, 1978). To this end, the goal of phenomenology is to describe experience as it

is lived.

Indeed, it is this lived experience that gives meaning to our world. Those objects and events that we perceive and interact with are meaningful to us. In our lived experience, we do not passively receive sense data, through our consciousness, we create a world which has meaning to us (Kohák, 1978). The world as we experience it is meaningful to us, not as a collection of objects but as our reality.

Husserl (1962) maintained, additionally, that as we make sense of our world through our consciousness, we are aware, not only of the particular phenomena we perceive, but also of the essences of those phenomena, that is, the necessary principles embodied by them. These essences (also called eidetic structures) are defined as the invariant principles within the experience. A classic example is that of a triangle, for despite the unique appearance and perspective of a particular triangle, we perceive and recognize it as a triangle. That is, our consciousness is able to grasp its "essence" - that it has three sides and a certain sum of angles (Kohák, 1978). Similarly, individuals may have experiences that are unique in many ways, but it is still possible to perceive the basic or essential structure of the general phenomenon.

The belief that experience contains essences and that these essences can be perceived if we only learn to see

clearly enough is a basic precept of phenomenology (Omery & Mack, 1995). In phenomenological research, the researcher attempts to identify the essences of the experience being studied. Indeed, this search for essences is the defining characteristic of a purely phenomenological study (Patton, 1990).

Because phenomenological inquiry is concerned with participants' lived experience, the method of data collection seeks to preserve the spontaneity of that experience (Munhall & Oiler, 1986). Therefore, most studies begin with unstructured interviews in which participants are encouraged to describe their experience in their own words. The original language of these accounts is recorded verbatim in order to maintain the context and meaning of the experience (Boyd, 1989).

Once the data have been collected, phenomenological analysis is performed. Although there are different approaches to this process (Omery, 1983), Spiegelberg (1982) has identified several common steps of the method. The first of these is investigating particular phenomena through processes referred to as intuiting, analyzing, and describing (Spiegelberg). Intuiting the phenomenon involves viewing the experience "through fresh eyes" so as to fully appreciate its uniqueness. To accomplish this, it is necessary to acknowledge one's pre-existing ideas about the phenomenon and then suspend them in order to understand

it as it is actually experienced (Kohák, 1978). Understanding that he or she comes with preconceptions about the experience, the researcher makes these preconceptions explicit and then attempts to set them aside in order to view the phenomenon as if for the first time (M. C. Smith, 1989). This process was given the mathematical metaphor of "bracketing" by Husserl, and it does not involve denying one's understanding of the world. Rather, it is similar to the suspension of the external world that occurs when we view a drama (Kohák). According to Husserl (1962), "The bracketed matter is not wiped off the phenomenological slate, but only bracketed" and is later reintegrated with a greater understanding of the subject (p. 194).

Analyzing the phenomenon involves comparing and contrasting the descriptions obtained, thus allowing the identification of the elements and structure of the phenomenon (Oiler, 1982). In this process, the particular experience is examined from different perspectives in order to get an appreciation of its uniqueness. Attention is focused on the context, the mode of consciousness - memory, perception, or imagination - and the specific elements of the experience (Polkinghorne, 1983). Spiegelberg (1982) calls this process "the general examination of the structure of the phenomena according to their components and their configuration" (p. 692).

In developing a description of a phenomenon, the investigator may make use of a variety of techniques, for example, comparing and contrasting instances of the phenomenon. Other ways of describing the phenomenon include making use of negation, analogy, and metaphor (Oiler, 1982). Using these approaches, the researcher develops a phenomenological description, the goal of which is "to serve as a reliable guide to the listener's own actual or potential experience of the phenomena" (Spiegelberg, 1982, p. 694).

The second step in phenomenological analysis is investigating general essences, which is the process of intuiting, analyzing and describing, not the particular phenomena, but the essence of the phenomenon under study (Spiegelberg, 1982). This essence, in Husserl's view, constitutes the meaning of the experience and thus is crucial to understanding it (Stewart & Mickunas, 1974). Finally, the analysis involves the discovery of essential relationships (Spiegelberg). These relationships may be within a single essence or between several essences. In order to understand these relationships, Husserl suggests the method of "free imaginative variation" (Spiegelberg). Using this technique, the phenomenologist imagines changes in various aspects of the phenomenon to decide whether or not its essence remains the same. The central characteristics that do not vary with the changes are

identified as the necessary and sufficient constituents of the phenomenon, or its essential structure.

When analysis is complete, the result is a comprehensive description of the essential structure of the phenomenon under study (Omery, 1983). In this study, the description of the experience of participating in clinical trials defines the clinical trial experience from the perspective of the participant and includes such information as: what it's like to be a participant in a clinical research project, how one comes to participate, what other people are involved in the decision to participate, how this participation affects one's life for better or for worse, and what meaning is ascribed to the experience. To be valid, this description should be so faithful to the experience that the participants in clinical trials can readily recognize it as true (Oiler, 1982). Two examples of comprehensive descriptions of lived experience can be found in Trice (1990), "Exhaustive Description of a Meaningful Experience" (p. 251) and in Cohen and Sarter (1992), "Summary Statement: The Meaning of Oncology Nursing" (p. 1485).

In phenomenological inquiry, there need be no attempt to interpret the findings, for description is "the clarification of the meaning of the objects of experience precisely as experienced" (Giorgi, 1992, p. 122). A complete description enables the reader to understand the

experience of participating in clinical trials from the perspective of the patients who are enrolled in them. The findings do not need to be interpreted, for they present a true picture of the experience as it is lived. They can then be used to enrich the knowledge base of nursing science by creating a greater understanding of crucial experiences within nursing's domain, to suggest further studies, or to drive practice (M. J. Smith, 1989). Kohák (1978) notes that the proper subject matter of a human science is the human being as subject and experience as reality. If this is the case, and if nursing seeks to understand human responses to health problems (American Nurses' Association, 1980), then phenomenological inquiry, as the most appropriate method for understanding human experience, is essential to nursing science.

For this study, using the phenomenological approach, the investigator turned to the phenomenon of interest, the experience of participating in Phase I clinical trials, and to those who had intimate knowledge of the phenomenon, the patients who enrolled in Phase I clinical trials. Participants were encouraged to freely describe their experience in unstructured interviews, which were captured on audio tape and transcribed verbatim. After analysis, a thorough description of the experience of participating in Phase I clinical trials was developed. The process and findings of this phenomenological study are described in

the chapters that follow.

Chapter 4: Research Design

The purpose of this study was to understand the experience of participating in clinical trials from the perspective of the patient; thus, the phenomenon of interest involved the mental/symbolic world rather than the physical world. Because of its domain, the study required the use of qualitative methods (Wolfer, 1993), and the phenomenological approach was chosen.

This study sought to identify the essential structure of the lived experience of participating in Phase I clinical trials from the perspective of the patient. It was assumed, then, that there is an essential structure to this experience which could be extracted from the patient's verbal description of it using phenomenological methods. That is, the assumption was made that, by analyzing individual patients' descriptions of their lived experience of participating in particular trials, it would be possible to identify the necessary and sufficient constituents of the experience of participating in Phase I clinical trials in general.

Definitions

For the purposes of this study the following terms were defined.

"Essential structure of the experience of participating in Phase I clinical trials" referred to the description of the central characteristics of the

experience of participating in clinical trials as identified by the patients themselves.

"Phase I clinical trials" referred to that designation given to a clinical research study the purpose of which is to establish the maximum tolerated dose in humans of a new anticancer agent or combination of agents. Phase I trials are carefully controlled by the National Cancer Institute or the pharmaceutical company that sponsors the drug. All studies complied with United States Food and Drug Administration regulations and met Institutional Review Board requirements for the protection of human subjects in the institutions in which they were administered.

"Patient" or "participant" referred to a cancer patient participating in a Phase I clinical trial who was over 18 years of age, fluent in English, and not personally known to the investigator prior to the interview.

Data Collection Procedures

A phenomenological approach was used for this study. The purpose of phenomenological research is to describe the experience of a given phenomenon by participants in order to identify common meanings across individual variations (Baker, Wuest, & Stern, 1992). In this way, a general description of the meaning of the experience of the phenomenon can be developed.

Phenomenology differs from other qualitative methods such as grounded theory in that no assumptions are made

prior to beginning the research. Rather than seek a conceptual framework for organizing the data, the researcher organizes and describes the data as they are discovered (Omery, 1983).

Setting

The study was conducted in a large metropolitan area of the western United States, in tertiary care centers where the clinical trials are administered. Since Phase I trials involve small numbers of patients, three different sites were used in order to make a larger sample available. Using different sites assumed that the phenomenon of interest, the experience of participation in Phase I clinical trials, had some central characteristics that do not vary with the setting. Common themes that emerged in spite of such differences were of particular value in identifying the shared aspects (or essential structure) of the phenomenon (Patton, 1990).

The interviews were conducted in the clinical area, in the participant's home, or in another location of the participant's choice. When interviews were conducted in clinical areas, within the limitations of the setting, every effort was made to insure privacy in order to encourage the participants to speak freely.

Population and Sample Size

The population consisted of individuals who met the criteria stated above for patients participating in Phase I

clinical trials. To be considered candidates for Phase I trials, these patients must have little or no chance of benefitting from existing therapies and must meet other eligibility requirements as determined by the particular trial. In general, these included the absence of serious comorbid conditions and a predetermined functional status as measured by a performance status scale such as the Karnofsky (Karnofsky et al., 1948). The sample was drawn from individuals who met the stated criteria and who agreed to be interviewed and tape-recorded. The sample was selected from the general population by primary selection; that is, based on the researcher's determination that they had had the experience being studied (Morse, 1991). The sample was not previously known to the researcher.

The sample was a purposeful or theoretical sample; that is, selected according to the needs of the study. In order to identify common experiences across participant and trial variation, a maximum variation sampling strategy was used (Patton, 1990). A deliberate effort was made to seek participants of both genders and different ages, diagnoses, and ethnic backgrounds.

In qualitative research, the sample is judged on appropriateness and adequacy. This sample was considered to be: (a) appropriate because it was composed only of participants who had had the experience of participating in clinical trials and (b) adequate because the data obtained

were relevant and complete (Morse, 1991). That is, interviews were continued until a thorough description of the experience had been obtained.

Specific sample selection criteria were as follows. Participants had to be age 18 or over and enrolled in a Phase I clinical trial. Additionally, they had to speak fluent English, consent to the interview, and agree to be tape-recorded. In order to participate, participants also had to have a Karnofsky Performance Status of 60% or greater, have no psychiatric history, and exhibit no cognitive deficits that would prevent their full and voluntary participation.

Exclusion criteria included a history of psychiatric illness, Karnofsky Status less than 60% or the inability to participate due to illness, and failure to pass a brief mental status examination (Appendix A). Also excluded were those participants whose command of English was too limited to allow them to fully understand and express themselves in that language. Participants previously known to the interviewer were also excluded.

The sample was recruited through research nurses and physicians conducting Phase I clinical trials. Potential participants were not approached until they had given consent to be contacted. Research nurses identified patients who met the eligibility criteria, told them about the study, and asked if they might be contacted. If they

agreed, then they were contacted, the study was explained to them, their questions were answered, and, if they desired to participate, they signed an informed consent document.

None of the patients approached by the research nurses or physicians declined to be contacted. One patient who was contacted about the study declined to participate. After the first interview, two participants refused the second interview, stating that they were dealing with advanced disease and wished not to be interviewed. Another participant did not return calls about a second interview.

The total sample size was 20, with 11 of the participants also giving a second interview. Despite the small sample, considerable linguistic data were generated, providing ample material for analysis. A total of 31 interviews were conducted for a total of 704 pages of transcripts. It was also assumed that each participant's verbal description was potentially a complete description of the experience and, as such, contained the essential structure of that experience.

Procedures

Data collection procedures included administering the Folstein Mini-Mental State examination, collecting demographic data, and then conducting unstructured interviews that were tape-recorded. Whenever possible, the participants were contacted for a second interview, either

in person or over the telephone. Second interviews were also tape-recorded. Details of these procedures follow.

Cognitive impairment is known to occur in cancer patients (Folstein, Fetting, Lobo, Niaz, & Capozzoli, 1984; Ganz, 1998) and could influence the validity of data collected. Therefore, potential participants for this study were evaluated for adequate cognitive functioning before being interviewed. After informed consent was obtained, the Folstein Mini-Mental State examination was administered to screen for any cognitive impairment (Folstein, Folstein, & McHugh, 1975). Since a score of 23 or less out of a possible 30 on this examination indicates cognitive impairment, a score of less than 24 excluded participants from interviewing (Folstein et al., 1984).

A tape-recorded unstructured interview format was used to elicit participants' verbal descriptions of their experience of participating in the clinical trial. This type of measurement is consistent with the phenomenological philosophy that in order to describe a phenomenon, one must make use of all data in the experience from the perspective of the participants. Omery (1983) wrote, "the concern of the phenomenological researcher is to understand both the cognitive subjective perspective of the person who has the experience and the effect that perspective has on the lived experience or behavior of that individual" (p. 50). Since measurement techniques must be guided by the intent to

preserve the natural spontaneity of participants' lived experiences (Munhall & Oiler, 1986), the unstructured interview was an appropriate technique.

Unstructured rather than structured interviews were selected because of their flexibility, which is necessary for discovery, and the opportunity they provide to immediately clarify the meaning of participants' responses. Unstructured interviews employ the phenomenological approach whereby most questions flow from the context of the participants' descriptions. Additional advantages of unstructured interviews include the opportunity to pursue complex processes and explore topics in depth as they are introduced by the participant. Skillful use of questioning also results in better response rates and more complete and accurate responses than does structured interviewing. Finally, unstructured interviews allow the immediate validation of the information with the participant, an essential means of enhancing the overall validity of the study (Waltz, Strickland, & Lenz, 1991).

There are some limitations inherent in the use of unstructured interviews, however. Interviews in general are costly in terms of time, money, and effort. Interviewer bias is a potential problem, more so with unstructured than with structured interviews. In addition, there is a possibility of the interviewer's impeding the interaction or preventing the discussion of sensitive

topics by his or her presence. Questionnaires that guarantee anonymity may elicit more valid responses on some topics.

Additionally, the lack of standardization in unstructured interviews means that systematic comparisons between participants cannot be made and that reliability in terms of repeatability may not be established (Waltz et al., 1991). However, in a study of this nature, where the goal is to describe the individual participants' experience as accurately as possible, reliability is not a major issue (Brink, 1991). Using repeated interviews over time and verifying transcripts with the participants themselves were used to increase both reliability and validity (Brink, 1991). In addition, the fact that all of the data came directly from the participants using their own words resulted in a more valid representation (Waltz et al., 1991).

All interviews were conducted by the principal investigator. During the interviews, participants were asked to describe how they came to participate in the clinical trial and what the experience was like for them. Since this was an unstructured interview, identical wording with each participant was not sought, and most questions flowed from the immediate context. However, the participants were encouraged to speak freely about their experience, and prompts were used to elicit information

about influences on their decision to participate, their expectations, and any changes in their quality of life as a result of the study. The participants were also instructed to describe their thoughts, perceptions, and feelings as completely as possible, and when no further clarification was required, the interview was considered complete. (Sample questions and prompts are found in Appendix B.)

Participants were interviewed as soon as possible after their enrollment in a Phase I trial and then, if possible, again several weeks to months later for a total of two interviews per participant. Repeated interviews were chosen to add depth to the material obtained, provide a means of determining consistency, and provide information on any changes in the experience over time. When available, transcripts of their earlier interviews were presented to participants for verification as well as clarification of details. This process helped to provide an in-depth picture of each participant's lived experience.

In addition to the interviews, another data source was field notes. These notes include descriptions of the setting, other people present, interactions that took place in recruiting participants and scheduling interviews, and any other observations that might be helpful in establishing a context for the interviews (Patton, 1990).

Demographic data were also collected by means of a questionnaire designed for that purpose (see Appendix C),

and information about the patient's disease was obtained from the patient, or in some cases, from the patient's nurse. These data were recorded but were not seen to affect the experience of participating in clinical trials with the possible exception of socio-economic status as discussed below. Therefore, it is assumed that, despite individual differences, there are shared aspects of the experience that were apparent across these variables.

Verbatim transcriptions were made of all tape-recorded interviews with each participant. The transcriptions were done by a transcriber hired for this purpose, with each transcript also reviewed and verified or corrected by the principal investigator. These transcriptions were then subjected to phenomenological analysis (Munhall & Oiler, 1986). The results obtained were validated by returning to the participants and asking whether the descriptions formulated contained the essence of their experience.

Data Analysis

The data obtained from the interviews were analyzed using phenomenological analysis. The steps employed in this analysis were: (a) reading and rereading the transcripts, (b) identifying constituents or meaning units, (c) relating these constituents to each other and the whole, (d) determining through this process the essential elements of the meaning units, and (e) integrating the essential elements into a consistent description of the

meaning of the experience. The participants were then consulted for validation that the final description was consistent with their experience.

To assist in the management of the data, a software program for qualitative analysis, The Ethnograph© was used. The transcripts were stored in The Ethnograph© files so that they could be easily accessed. The data were then coded using the typed transcripts, and these codes were also entered into the data files, allowing sorting of the data using search procedures.

Briefly, the phenomenological analysis involved a number of steps that aimed to determine the essence of the phenomenon of participation in clinical trials. Using one of the methods described by Omery (1983), the following steps were followed.

First, the interviews were transcribed verbatim and all were read to get a sense of the whole. In this step, the texts were reread as often as necessary to become thoroughly familiar with them, a minimum of three times. This step served as a ground for the next step (Giorgi, 1985). Next, the material was read again more slowly and units in the experience that are called constituents were identified. Constituents are meaning units that are identified when there is a change of meaning of the situation for the participant which seems relevant to the phenomenon being examined (Giorgi). These meaning units

were coded by the researcher, using the participant's own words and phrases wherever possible. The codes identified were then entered into The Ethnograph© files. What stands out as constituents depends, of course, on the researcher's perspective - in this case, a desire to understand the meaning of the experience of participating in clinical trials. After identifying constituents, redundancies were identified and the remaining constituents were clarified by relating them to each other and to the whole. The Ethnograph© software facilitated this step by simplifying the comparison and contrast of coded units of experience in the various transcripts.

At this point, through reflection and imaginative variation, the concrete language of the participants was translated into the language or concepts of science. That is, the essential elements of each particular meaning unit were determined and summarized (Giorgi, 1985). The significant themes were now no longer expressed in the participants' own words but were described using a more general scientific language.

Finally, the insights were integrated and synthesized into a consistent description of the meaning of the experience. All of the transformed constituents are at least implicitly contained within this general description (Giorgi, 1985). At this point, the final description was validated by other researchers who examined the summary

description for consistency with the data, and by returning to the original participants to see if it was faithful to their experience (Omery, 1983). An example of the procedure used in phenomenological analysis may be found in Table 1.

Constituent Identified	"I'm hoping and...I'm an optimist....That somehow someway the PSA will drop and if that doesn't happen maybe they can stabilize things where I can look forward to at least, I don't know how long, but, you know, at least buy some time."	
Code Assigned	BUY TIME	
Restatement	Participation in a clinical trial for the purpose of extending the participant's remaining time to fulfill a specific goal or to find new treatment options.	
Comparison with Another	Ed Woodward: "...at least buy some time."	Margaret Gross: "If it gives me another year or two, there's something else out there."
Identification of Theme	Theme: The Quest for Treatment Subcategory: Hope, Extension of Life	
Inclusion in Final Description	Treatment on a clinical trial represented...the hope of extending the time left to them.	

Table 1: Example of Decision Trail for Analysis

Protection of Human Subjects

Prior to collecting pilot data, approval was obtained from the Human Subjects Protection Office of the University of California, Los Angeles and from the institutional review boards of the institutions from which participants were recruited. In addition, the rights of participants

were protected in several ways. First, it was stressed to potential participants that participation was strictly voluntary and that they could withdraw from the study at any time (see informed consent forms in Appendix D). Those not consenting were not interviewed. Second, although the interviewer necessarily knew the identity of the participants interviewed, confidentiality was maintained by recording and storing participant names and data separately. Finally, any identifying demographic data were removed or disguised in presenting the findings.

In order to protect participants from harm resulting from the interviews themselves, participants were screened for limitations due to illness or fatigue and for cognitive impairment before interviewing them. Before beginning the interview, the participants were assured that their participation was voluntary and that they could discontinue the interview at any time. Additionally, participants were carefully observed for signs of fatigue or distress and the interview was ended if such became apparent. On two occasions the interviewer did end the interview because of participant fatigue. On two other occasions, the interviewer offered to end the interview because the participant had begun to cry, but on each occasion the participant urged the interviewer to continue. While there is evidence that participants are not harmed by such interviews and may actually benefit from the opportunity to

tell their stories (Hutchinson, Wilson, & Wilson, 1994), the possibility remained that material discussed might have provoked an emotional reaction in the participant (Ramos, 1989). Therefore, arrangements were made for appropriate referrals for those participants whose emotional distress warranted it. None of the participants, however, felt the need for additional counseling because of the interviews.

Validity

"Valid interview data are those that accurately portray what the investigator is attempting to study" (Hutchinson & Wilson, 1992, p. 117). There are several potential sources of invalidity in the interview. For example, there may be a lack of commonly comprehended meanings (Waltz et al., 1991). To guard against this threat, care was taken to use language that was understandable and part of the frame of reference of the participants (Patton, 1990). In particular, medical terminology was avoided. Additionally, there was, as has been noted, variability in settings and situations (Waltz et al., 1991).

Other threats to validity include reactive effects, demand characteristic effects, and reverse-demand characteristic effects (Waltz et al., 1991). Reactive effects are present when participants modify their responses just because they are being interviewed. Demand characteristic effects reflect the participants' attempts

to respond as the interviewer desires, while reverse-demand characteristic effects occur when the interviewer attempts to convey preconceived meanings to the participants. Careful attention to the wording of questions was used to minimize these sources of invalidity (Waltz et al.). Rapport was established with the participants while neutrality was maintained with regard to the content of the interview, a method helpful in reducing these threats (Patton, 1990).

Also in order to increase validity, pilot testing was done with the first participant who met the criteria. During pilot testing it was determined that the questions asked were acceptable and comprehensible and that they allowed the participant to answer fully. It was also found to be helpful to have the participant give some history of previous treatment before coming to the clinical trial. Therefore, the typical questions were retained and subsequent participants were asked to give a little history as a background to their participation in the Phase I trial.

Interviewer bias can be a source of constant error that threatens the validity of the measure (Brink, 1991). For example, the interviewer may ask questions in a language that is rooted in previous knowledge (May, 1991). An example would be to ask the participants about "informed consent." Or the interviewer may subtly influence the

discussion through the use of language. Techniques to control such bias included using open-ended questions in nonspecific language until the participants' own terms could be defined (May, 1991), and consciously maintaining an open attitude as free of preconceptions as possible (Rew, Bechtel, & Sapp, 1993).

As discussed previously, the phenomenological method requires that the researcher identify and acknowledge any preconceptions about the phenomenon of interest. For this study, I acknowledged my impressions that participants in clinical trials are motivated by such factors as hope, altruism, and the expectation of personal benefit. I also recognized my previous experience with clinical trials and my knowledge of both the nature of Phase I trials and the low probability of objective tumor response in these trials. In addition, prior to each interview, I attempted to bracket, that is, set aside, my previous beliefs in order to capture the participant's unique experience. These attempts and other impressions were recorded in the form of memos attached to the interviews. Because, in phenomenological studies, the researcher uses him- or herself as the primary instrument for data collection, close attention also was paid to such attributes as authenticity, credibility, and sensitivity (Rew, Bechtel, & Sapp, 1993). Transcripts were periodically reviewed by the dissertation chair and by researchers skilled in cancer

nursing and phenomenological methods. As a result of this feedback, an attempt was made to use less structured questions in order to elicit the participants' own responses.

To ensure that data were not lost in the interview process, sufficient time was allowed for each interview (up to two hours), and the entire session was tape-recorded. In addition, the tapes were transcribed as soon as possible in order to capture and record any additional ideas, nuances, and observations of nonverbal behaviors while they were fresh in the interviewer's mind (Hutchinson & Wilson, 1992). In qualitative studies, credibility is analogous to internal validity. A credible study is one that presents such a faithful description of the phenomenon that a person having the experience would immediately recognize it from the description (Sandelowski, 1986). In the process of analysis, each step was validated by referring back to the original data, both the audio tapes and the transcripts. Also, a draft of the final description was validated by referring it back to three of the original participants, a 50-year-old woman with melanoma, a 50-year-old man with lung cancer, and a 64-year-old woman with colon cancer. Two of these participants stated that they agreed completely with the summary statement, noting "I agree 100%," and "I can't think of anything to add." The third participant agreed with the statement generally but

could not relate to the idea that his participation in the trial might benefit others in the future because, he maintained, cancer treatment is changing so fast that his particular treatment, a combination of chemotherapy agents, would not be used in the future. The theme of benefitting others by their participation was so pervasive in the interviews, however, that it was left in the final summary statement. Other comments made by these participants were incorporated into the description.

In addition, care was taken to avoid researcher bias in the description of the phenomenon by explicating my perspective as the researcher, bracketing preconceptions, and interviewing unfamiliar people (Oiler, 1982). In the bracketing process, the phenomenological researcher engages in the process of reduction, a process of separating oneself from one's preconceptions in order to perceive the essence of the phenomenon under investigation. That is, the goal is to describe the real, lived experience without interpretation and explanation.

Reliability

Reliability as a measure of consistency does not usually apply to a qualitative study. Reliability, used in the quantitative sense, may actually undermine validity in the qualitative sense (Sandelowski, 1986). For example, Polit and Hungler (1991) have stated that "imposing structure on the research situation (e.g., by deciding in

advance exactly what questions to ask and how to ask them) necessarily restricts the portion of the participants' experiences that will be revealed" (p. 498). However, a form of equivalence was established with the interview data by using identical or alternate form questions with the same respondents. This procedure helps to establish the equivalence of the data regardless of the form of the question. Additionally, the use of tape recording provided an alternate form of data recording other than memory and written notes (Brink, 1991).

Consistent with recommendations for qualitative methodology, auditability was also considered. Auditability is demonstrated in the research report when another researcher could arrive at the same or comparable conclusions given the stated data, perspective, and situation (Sandelowski, 1986). To enhance auditability, the reasoning process of the analysis must be clearly described (Burns, 1989). In order to document coding and analytical decisions, records were kept of sampling decisions, decision rules for transforming data to higher levels of abstraction, and responses of participants to transcripts and the descriptions developed from them (Burns, 1989). These records were kept in the form of field notes as well as observational, methodological, and theoretical memos, excerpts of which are included in the section on conducting the research. These data facilitate

a reader's following the "audit trail" and judging the auditability, or consistency, of the study.

Finally, reliability of data analysis was addressed. Sources of random error include "missing data, coding errors, misinterpretation of data, and miscoding due to judgement error, unclear or illegible notes, poor transcriptions, and so on" (Brink, 1991, p. 179). In order to guard against these sources of unreliability, coding was checked by other researchers knowledgeable about the procedure. An expert panel of nurses familiar with both the population and the methodology validated samples of coding at 81%. The same group of expert nurses also validated the logic of the final categories, with 100% approval. In addition, the test-retest method of recoding the material after it has been allowed to sit for a period of days was used (Brink, 1991).

This study generated a comprehensive description of the experience of participating in Phase I clinical trials from the perspective of the patient. Because the participants interviewed were patients having this experience, and care was taken to ensure methodological rigor, the description can be considered a valid representation of the effect of clinical trials on these participants' lives. The phenomenological approach allowed the researcher to gain insight into the clinical trial experience that may be used to broaden the knowledge base

of investigators conducting clinical trials and nurses providing care to patients on trials. The understanding gained may assist clinicians in providing accurate, meaningful information to patients recruited to clinical trials as well as appropriate support throughout their participation.

Conducting the Research

In qualitative research, the researcher "not only collects data but also serves as the 'instrument' through which data are collected" (Rew, Bechtel, & Sapp, 1993). A description of the process of conducting the research using myself as the instrument is essential in establishing the validity of the data presented. This section will describe some of the approaches, reflections, and decisions I used in data collection and analysis.

The motivation for this study came from my experience working with patients who were on clinical trials. As a staff nurse, I worked in a research facility and saw a number of patients who were on investigational treatment. I was curious about patients' motivation for going on trials and about the ways in which their quality of life might be affected. As an oncology nurse, I was concerned about whether the risks associated with clinical trials justified the benefits, especially in the early trials. My own experience as an oncology nurse and my concern for my patients' welfare contributed to my authenticity as a

researcher (Rew, Bechtel, & Sapp, 1993).

When I began reviewing the available literature, I found that studies had not yet addressed the issues of patients' experience and the meaning that it held for them. Given the lack of knowledge in the field, I decided to use a phenomenological approach in order to discover patients' lived experience. Phenomenological research relies on interviews as a source of data (Hutchinson & Wilson, 1994); I determined to interview 20 participants who were taking part in Phase I clinical trials.

Before I began interviewing participants, I bracketed or set aside, my preconceptions in order to be open to participants' own experience. At that time, I recorded my belief that "personal benefit may not be the most important consideration for some patients who enroll in clinical trials. Hope and altruism...may both play a role in their participation." I also noted that patients might be motivated by the desire to please their family or health care team. In addition to the bracketing I recorded before beginning the study, I kept memos of my impressions, decisions, and awareness of the developing themes throughout the course of data collection and analysis.

I used unstructured interviews to encourage participants to describe their experience in their own words. Since I regularly conducted interviews with patients in the course of my practice, it was also a

familiar and comfortable technique for me.

Hutchinson and Wilson (1994) wrote that both therapeutic and research interviews rely on the following: (a) establishing rapport with the participant/client, (b) using open-ended questions to encourage free expression, (c) striving for accuracy in description, (d) demonstrating sensitivity and judgment, (e) maintaining confidentiality, and (f) remaining objective. The differences between therapeutic and research interviews lie in the purpose of the interviews, the theoretical perspectives used, and the participants' motivation. In conducting interviews with my participants, I relied on my experience as a nurse, but always kept in mind the purpose of the interview and tried to adopt a researcher rather than a clinician role. To do this, I maintained neutrality with respect to the information patients shared with me, did not offer my services as a nurse when there was an opportunity (for example, when participants had questions or concerns related to their treatment) and tried to remain open to learning from the patients' experience rather than my own.

When participants asked specific questions, I either referred them to their physician or nurse or deferred the question until the interview was over. In that way, I attempted to keep my roles separate. On rare occasions, however, a participant showed such concern that I responded more therapeutically because I felt that patient advocacy

took precedence over the research at that moment (Rew, Bechtel, & Sapp, 1993). I also used my clinical judgment to end the interview whenever the participant appeared tired. In this way, I tried to maintain "the delicate balance between flexibility and consistency, depth and breadth, and...get the story and attend to the needs of the storytellers themselves" (May, 1991, p. 200).

Because my participants were on investigational protocols, they spent many hours at the hospital for treatment and observation. Several participants suggested that they would prefer to be interviewed in the clinical setting, since they were required to be there anyway. With the permission of the staff, I was able to conduct many interviews at the hospitals. As a nurse, I was aware of the need for medical procedures and could avoid interfering with the work of nurses and physicians, and the staff were very helpful in assisting me to provide privacy. On several occasions, my participant was given a private room or cubicle so that I could conduct the interview.

I brought my credibility as an oncology nurse to the interviews. I was able to quickly establish rapport with the participants and they came to trust me. I understood their disease and the treatment they had had. Because of my credibility, participants spoke freely about their experiences.

When I had conducted the first three interviews, I

recorded, "I am coming to feel that patients seek clinical trials in greater numbers than I had supposed. It is known that AIDS patients seek trials, but that cancer patients do the same is not, I believe, generally known." This passage was my first mention of the major finding of this study, the Quest for Treatment. As the research proceeded, I continued to use my intuitiveness to develop a picture of the whole experience of participating in Phase I clinical trials (Rew, Bechtel, & Sapp, 1993).

Although the aim of the study was to describe the experience of participating in Phase I clinical trials, participants also shared information about their past cancer treatment, their family lives, their work, and their feelings of hope and despair. I felt privileged to listen to their stories, and I often had the feeling that, for all my years of experience in oncology nursing, I was learning more about having cancer than I had ever known before. For example, two of my participants told me that they would not take their antiemetic because it made them too drowsy to carry out normal activities. I had previously thought that relief of nausea was a top priority for all patients. My receptivity and willingness to learn from my patients helped me to discover the common meaning in this experience (Rew, Bechtel, & Sapp, 1993; Sandelowski, 1986).

There were several times in the course of the interviews that I had to make a decision about how to

proceed. The first decision point arose in the third interview when the participant's mother entered the room and added some of her own comments. Although I had wanted to hear the participant's perspective, I did not ask her mother to leave but continued to record. In that way, I preserved both the participant's comments and the context in which they occurred. In the following interviews, I asked the participants before the interview if they cared to have their family member or friend present, and if they were comfortable, I allowed visitors to remain. I also repeated my promise of confidentiality to both the participants and their family members.

The decision of whether or not to hold a second interview was made entirely by the participant. Two participants who suffered disease progression after they came off study declined second interviews. Other participants died after their first interview, and one developed brain metastasis. This participant at first stated that I could interview her "if you will be patient and go slow," but then admitted that she was not able. She said, "I remember you, Carol, but I don't remember anything else." When I contacted a participant for a second interview and did not get a return call after two messages, I did not pursue the issue. Out of 20 participants, 11 were able to give second interviews.

In the second interview, I sought to confirm

information from the first interview by asking the same questions related to the search for treatment and the decision to enroll in a clinical trial. In addition, I asked about their experience since coming off study. I found that participants were more open about their feelings in the second interview, especially about their feelings related to the uncertainty of their condition. I was able to get a different perspective that enriched my findings. I enjoyed these second interviews. Although I spent a limited amount of time with these participants, I came to care for them and was concerned about them and anxious to see how they were doing. I was privileged to share a significant time in their lives and I developed a relationship with them.

I also talked with the research nurses who had referred patients to me. They were able to give me information about the participants' conditions and to confirm their deaths when they occurred. Although I was always saddened to hear of a participant's death, I was glad to have the information and to know whether they had completed their goals before death. One participant, for example, lived long enough to see his son married, a goal he had shared with me.

Another participant confided that she had never been baptized although she had been raised with a Protestant faith. Now that her lung cancer was advanced, she wished

to be baptized but had been unable to make the arrangements. After our conversation, I gave her a referral to a pastor who I knew would be willing to baptize her. This participant died suddenly while on treatment and had not contacted the pastor when she died.

After I completed the interviews, I spent many hours reviewing both the tape recordings and the written transcripts. I had noted that most of the participants found their clinical trials through their own efforts. This Quest for Treatment became the major theme arising from the data. As I reflected on the data, I recognized other categories and themes that were repeated over and over again in different words by the participants. I began to develop a picture of the essential characteristics of the experience of participating in Phase I clinical trials.

As I worked with categories and themes, I consulted with a number of colleagues who helped me to refine my analysis. When I had constructed a description of the experience of participating in Phase I clinical trials, I read it to three of my participants. They confirmed that the findings represented their own experience. In the next chapters, I present these findings.

Chapter 5: Overview of Findings

The purpose of this study was to explore and describe the experience of participating in Phase I clinical trials. Cancer patients participating in such trials generously contributed their time and willingly shared their perceptions of their experience in a series of interviews. These participants differed in many ways, but they shared the common experience of being a subject in a Phase I clinical trial. The findings presented here represent the essential structure of that shared experience.

Sample Characteristics

As noted, a maximum variation sampling strategy was used in an attempt to recruit participants of both genders and a range of ages, diagnoses, and ethnic backgrounds. The participants ranged in age from 35 to 77 and came from a variety of backgrounds. However, all but three were non-Hispanic caucasians; there was, therefore, an underrepresentation of minority ethnic groups in the sample just as there was in the Phase I trials from which the participants were drawn. (Please see Table 2.) All of the patients declining to participate were private patients and were similar demographically to those who did participate, with the exception that one was Hispanic.

The participants were well educated and reasonably affluent. All had completed high school and 17 of the 20 had at least some college education. Additionally, over

Age		Marital status	
30-39 yrs	1	Single	4
40-49 yrs	3	Married	9
50-59 yrs	8	Widowed	2
60-69 yrs	6	Separated	0
70-79 yrs	2	Divorced	5
Gender		Education	
Male	9	< High school	0
Female	11	High school grad	3
		Some college	9
Ethnicity		College graduate	8
Caucasian, non-Hispanic	17	Household income	
Hispanic	2	<$15,000	1
African-American	1	$15,000 -30,000	5
		$30,001 - 45,000	2
Employment status		$45,001 - 60,000	1
Full-time	8	>$60,000	8
Part-time	0	Declined to state	3
Unemployed	2		
Retired	6	Primary cancer diagnosis	
Disabled	4	Ovarian	2
		Breast	2
Religion		Melanoma	6
Protestant	5	Lung	6
Catholic	5	Prostate	2
Christian	1	Kaposi's sarcoma	1
Jewish	5	Colon	1
AA Spirituality	1		
None	3	n = 20	

Table 2: Demographic Characteristics of Sample

half of the 17 participants who volunteered information on their household incomes earned more than $60,000 a year. Participants also met the criterion of a Karnofsky Performance Status of at least 60%, which represents being unable to work but able to care for most of one's own needs (Karnofsky et al., 1948). Eight of the participants were employed full time, and only four considered themselves to be disabled.

In addition to performance status, participants demonstrated adequate cognitive functioning by passing the Folstein Mini-Mental State examination with a score of 24 or higher. On this test, no participant scored less than 26 and all but one scored between 28 and the maximum of 30.

Most participants on Phase I clinical trials fail to show an objective response (Estey et al., 1986; Von Hoff & Turner, 1991). The overall response rate for these participants, according to information from them and their research nurses was 2/20 or 10%, with one participant lost to follow-up. A total of 13 failed to respond to treatment, 4 are known to have died and 3 more were terminally ill at last contact. Only 2 were still on study at the time of the second interview and 3 more had completed the study and had stable disease. (Please see Table 3.)

Years since diagnosis:		Results:	
< 1 year	3	Failed, alive	9
1 - 5 years	11	Failed, died	4
> 5 - 10 years	3	Completed, stable	3
> 10 years	3	On study, stable	1
		On study, response	1
Type of trial:		Off study, response	1
Combination chemo	5	Unknown	1
Biological	8		
New agent	7	n = 20	

Table 3: Participant Responses to Phase I Trials

The Quest for Treatment

In an interview, Jane Martin* described her attendance at a support group for cancer patients and what

she learned from the discussion there:

> A lot of our time is spent in looking for trials. Especially, of course, the patients, where either they had an unusual cancer or they hadn't responded to regular treatments. And that seemed to be an underlying thing of, "How do we find the trial, are we lucky enough to find one that we qualify for." So it's something that cancer patients who are a little out of the realm of regular cancer where there's regular treatments for - they really live for these trials - not live but they're hoping to look for these trials. I mean, this is their whole hope. To get into a trial. Because to them that's the only treatment they have available a lot of times.

*Note: In order to protect the confidentiality of the participants, all names are fictitious and all identifying information has been altered in the accounts drawn from the interviews conducted for this study.

This data segment illustrates the most striking finding of the study and introduces the overall theme that emerged from the interviews, namely, the Quest for

Treatment. This theme unfolded in the typical response to the first question of the interview, "Please tell me a little about what has happened to you since you were diagnosed and how you came to participate in this trial." Most participants, like Ms. Martin, told of being diagnosed with cancer, exhausting standard treatment and then beginning a quest for additional treatment, including clinical trials. Most often, this quest was undertaken independently by the participant; sometimes the participant's oncologist was involved. Of 20 participants, only 7 were referred by their physician to the Phase I trial; the rest found the study through their own efforts. Of these, five specifically mentioned using the Internet, four used the connections of family members or friends, and the remaining four stated only that they had done "research" to find out what was available.

Some of the participants were referred to their Phase I study by physicians after they had researched the hospital or the physician on their own. Many participants told of choosing a major treatment center because they felt that there would be more treatment options available to them and that they would receive the latest therapy. Christine Braun, a 60-year-old woman with ovarian cancer, stated:

> I still believe...that if you go to the universities, they really will give you the best,

> what is available at least, you know, and I always feel also that maybe with one treatment you will not find what you are looking for, you have to try and see what will work for you, you know.

This woman's cancer recurred after she had participated in a Phase I trial of combination chemotherapy. At the time of her second interview she was on another type of chemotherapy and remained hopeful that other options were still open to her.

Several participants mentioned that upon initial diagnosis, they were far more willing to follow their physician's recommendations but that, over time, they became more proactive in their search for appropriate treatment. Margaret Gross, a woman who had been diagnosed with breast cancer 8 years previously provided an example. When she was first diagnosed, she said, "I did what I was told." Then, when the cancer recurred and she had a bone marrow transplant, she became more active in her own care, joining a support group that also provided information to cancer patients. It was through this group and by accessing the Internet that she found the Phase I biotherapy trial in which she was enrolled.

This pattern did not hold for all patients, however. The time from cancer diagnosis for patients interviewed ranged from less than 1 to more than 18 years. Some had

pursued investigational treatment immediately. These patients, however, were those with advanced lung cancer and with melanoma, diseases for which standard therapy offers little hope of cure. Thus, a patient seemed to make the decision to seek clinical trials only after exhausting all available standard treatment options.

One Participant's Story

The Quest for Treatment is illustrated by the following description of one participant's experience of participating in a Phase I clinical trial.

Jane Martin is a 50-year-old married woman who discovered a mole on her right thigh two years ago. A biopsy revealed malignant melanoma. After an initial wide excision, she received no further treatment until she had a recurrence a year and a half later. Following another wide excision, she was advised to be watched closely, but no other treatment was recommended. At that point, she and her husband decided to seek other opinions. Unfortunately, they did not get a consensus. Some physicians recommended interferon therapy, others felt that close observation was adequate. One oncologist recommended a limb perfusion procedure. Radiation therapy was also mentioned.

At that point, the Martins started using the Internet and also called the National Cancer Institute's Cancer Information Line looking for any trials anywhere in the country for which she might qualify. After receiving a

list of current trials, she faxed a copy of her medical history to each doctor and hospital listed. More than half of the physicians she contacted responded. Eventually, she spoke to an oncologist doing Phase I biotherapy trials at a major cancer center in another state. This physician explained the trial over the phone and said that he felt it could be of benefit to Ms. Martin. He then sent written information which Ms. Martin and her husband read and shared with her physicians. In addition, the protocol nurse faxed them a copy of the informed consent form. Then, having weighed the risks and potential benefits of the treatment as well as the expenses of travel, they decided to go ahead.

Ms. Martin described her decision to go ahead with this Phase I trial in terms of needing to "do something." She described lying in bed at night, wondering if the cancer would recur and if it did, how she would feel if she had not done something about it in terms of treatment. She and her husband also considered the risks associated with this particular treatment and consulted with her physician who agreed with their choice of treatment because he believed the risks to be minimal.

When asked if she had any feelings about being a research subject, Ms. Martin stated that although her primary motivation was to help herself, she had also considered that by participating in the research, she might

also be helping future patients, perhaps even her own family. Being part of that effort felt good to her.

Ms. Martin tolerated her treatment very well. At last contact, she had completed the trial and had not had a recurrence of her melanoma. When asked if her participation in the trial had affected her quality of life in any way, she stated that she had achieved some peace of mind in knowing that she was doing something about her disease.

Although Ms. Martin had completed her Phase I trial, she had not ruled out the possibility of further treatment, even another investigational treatment, especially if her melanoma recurred. Her husband was still spending at least an hour a day on the Internet searching for other options.

The Martins were convinced that it was up to them to pursue treatment options because of the lack of consensus about treatment among the physicians they consulted. They were frustrated by the lack of direction they received as well as by the inherent uncertainty in her situation. She was terrified of a recurrence, but her husband was prepared. He cited several trials in various parts of the country that seemed promising to him.

The Martins were not unusual in the sample of participants who were interviewed. They faced the fact that standard treatment had little to offer in their situation, they took charge of finding out about other

treatment options, and they took action to make sure that she had treatment. They continue to search the Internet for promising trials and will certainly continue to take an active role in her treatment.

Chapter 6: Steps in the Quest

The Quest for Treatment was seen as an active process that follows a typical course, marked by steps along the way. These steps emerged as categories across the narratives: (a) Taking Charge, (b) Deciding, (c) Living on a Trial, and (d) Dealing with Uncertainty. (Please see Table 4.)

Taking Charge >	Deciding >	Living on a Trial >	Dealing with Uncertainty
	Decision Process	Quality of Life: Physical Social Psychological Spiritual	
	Hope: Extend life Not to die Cure Improvement Nonspecific	Meaning	

Table 4: Essential Themes of The Quest for Treatment

Taking Charge

For the participants interviewed, the first step in the quest for treatment was taking charge of their own care. They stated that they realized they needed to find their own treatment and began a search, looking for options. As indicated above, the participants generally reached this stage when they were told that they had no more standard treatment available or when they were told that nothing more could be done to treat their disease.

These participants decided to take charge of their own fate for several reasons. Some felt that they lacked direction from their physicians. Jane Martin described her experience:

> I think that was my hardest part of the summer. Not just deciding what to do but how, you know, it's not like the doctors came to you and said, "This is what we think you should do and this is the information and you can do it or not."

She felt that "it was really our decision and that is hard." Another participant, Sharon Barnes, agreed. After being given conflicting advice by her physicians, she said, "I think people are finding out more themselves...than the help they're getting from their own doctor." These patients, then, frustrated with the guidance they received from physicians, decided to seek options that had not been presented to them.

Other participants simply rejected the advice given them by their physicians. They expressed the feeling that they knew more about what was good for them than their physician did. Shirley Palmer, a woman with metastatic colon cancer put it this way, "You have to get out there and do your own thing. And yet, I guess, I've been able to understand more the feeling that I know my body better." Another example comes from the second interview with Margaret Gross, a woman who had had extensive prior

treatment during an 8-year battle with breast cancer. When she returned to her community oncologist after having been taken off the Phase I trial she was on because of progressive disease, he recommended a course of chemotherapy that Ms. Gross felt was too toxic for her. She vehemently rejected his recommendation:

> After I failed the [Phase I trial], and [my doctor] wanted me to go on...this course of chemo, my natural mind says, "I'm too healthy for this fuckin' son of a bitch to do this to me!" And I said, "No, you're not gonna do that to me, you're not gonna take me down again," and I said, "My body's too healthy." And I went for somethin' else.

Another participant described her encounter with the surgeon who had removed a recurrent melanoma from her leg:

> Dr. N. said, "I thought you were gonna go have that limb perfusion done." And I said, "Well, I don't feel good about that." And he said, "Sharon, you have to do something." And so I said, "Well, what am I supposed to do?"

At that point, she began looking for other options herself.

Participants also consistently rejected their physicians' statements that there was nothing else that could be done for them. Thomas Williams, a 59-year man with advanced lung cancer said it this way, "That

was...when I decided, you know, there ain't nothing you can do for me, then I gotta go someplace else."

Mark Stewart, a 35-year-old man with Kaposi's sarcoma, stated that he had always believed that there was more treatment available "until this last time when they actually verbally said...you've pretty much done everything that you can do." Although he did recover from that acute episode and was offered more treatment, he was forced to consider that his options were limited. Asked what his response would be to finding that no more treatment was available, he replied, "I haven't thought about it, I would probably go somewhere else."

This belief that there is more or better treatment available somewhere else was a common theme in the interviews. Several participants specifically stated that they believed that the right treatment for them was somewhere "out there." For example, Mary Hogan, a woman with breast cancer, described how she researched available treatments. "At the time, I was interested in knowing what was out there. I actually started doing this after my reoccurrence in '92." Margaret Gross also stated, "I knew there had to be something else out there, I went after it, okay?" Another participant, Albert Paredes, a 53-year-old man with lung cancer, expressed the same attitude when he said, "I just thought there's gotta be something better out there."

Determined to find treatment, even investigational treatment, these participants made use of all the resources available to them. A third of the participants specifically mentioned searching the Internet for trials. Willard Holmes, a man with recurrent melanoma, stated that, "I was aware of other, you know, Phase I trials going on around the country. I had done a lot of research on the Internet." Similarly, Thomas Williams told how he found a clinical trial: "I think my wife picked it up off the Internet. She's been searchin' the Internet for stuff." Shirley Palmer reported, "My husband has been working on the Internet, picking up these various studies around the country." The Internet, then, was a popular source of information on available clinical trials.

Another popular source of information was the National Cancer Institute's information line, 1-800-4-CANCER. Mary Hogan said, "I read. I called the National Cancer Institute a lot," and Sharon Barnes stated, "I had called the national cancer line and had her send me all the materials on, on the vaccine, or any treatment that was being done for recurrent melanoma." Jane Martin used both resources: "I had been using the Internet and had somehow connected with the cancer hotline and asked them if there were any trials going on anywhere in the country that I might be eligible for."

Many participants also used personal and family

connections to assist them in finding a trial. Mabel Scott, a 77-year-old woman with recurrent ovarian cancer, had a daughter who worked at a major medical center. She said her daughter "insisted that I come there since she had known Dr. B." Another participant related, "I have a brother who is very successful on the East Coast. He sits on a number of corporate boards, and he hooked me up with a doctor."

Participants also mentioned networking with others as a source of information. Willard Holmes explained,

> I have friends and just my own network of people out there that, you know, watch for articles in papers and stuff and they see something, they clip it and send it to me and I usually call and follow up and see what it is.

Similarly, Shirley Palmer reported that she discussed the clinical trial with her family and with "just about everybody we know. They all were searching for me and if there was anything in the paper, on the television, 'Did you hear this one on the radio?'"

For the participants, Taking Charge meant declining to follow their physicians' recommendations, taking the initiative in finding treatment, and using their own resources to seek out trials. For some participants, Taking Charge arose from frustration with the lack of assistance from their physicians; for others, it was a

reflection of their growing need to be involved in their own care. Taking Charge and searching out treatment options lead the participants to Phase I clinical trials.

Deciding

Once the participants had located a clinical trial, the second step, Deciding, began. One question of interest in this study was how patients decide to participate in Phase I clinical trials and what factors influence their decision. Under the category of Deciding, there arose two essential themes, the Decision Process and Hope. The Decision Process comprised reading the trial's protocol, asking questions, and completing informed consent procedures. Hope described the theme of anticipation of benefit from the trial.

The Decision Process

Participants described learning about a Phase I trial and being given information about it in the form of a protocol or informed consent form. This information was often conveyed by a research or protocol nurse rather than the physician. Participants then reported reviewing the information before deciding to participate. Most (13/20) participants read the protocol and informed consent form carefully, but 3 reviewed it in a cursory manner, having already made up their minds to enroll.

Mabel Scott was a 77-year-old woman with recurrent ovarian cancer. She described the decision process in this

way:

> And they, they gave me the protocol to read through...And I spent quite a bit of time readin' it. A lot of it I didn't quite understand, but, because of the medical terms and this and that and the other, but when it was all over with, why it was simpler than I thought to start with.

In another interview segment, Ed Woodward, a patient with prostate cancer related his experience of enrolling in a trial on which a patient death had occurred:

> My wife and I discussed the program at length. We read the protocol several times and liked the way they spelled everything out...this was the revised version and M. [the research nurse] indicated as much, that there were some changes made from the original protocol because of...what had happened; and I said "Let's give it a try."

Like Mr. Woodward, most participants stated that, after reading the protocol, they had a good idea of what to expect from the study. Laura Thompson, a woman with lung cancer, related, "I read it and I understood what could happen and what may happen and what may not happen." They felt that they had received adequate information to decide whether or not to participate, and, later, when asked if anything had surprised them about the study once they started, most stated that they had had no surprises, since

they had known what to expect.

However, when participants still had questions after reading the protocol or consent form, they requested additional information. Mary Hogan, for example, noted, "I read the protocol several times...it's involved, so I didn't completely get it, and so I had Dr. W. re-explain it to me." Another participant, Mabel Scott, who had been given information by a research nurse, refused to sign the informed consent form until she spoke with the physician: "And so I had all these papers that I was to sign and in the paper...it said something about your doctor has explained all this and he hadn't explained a darn thing, and I refused to sign it."

Some participants brought family members or friends to ask questions for them. Michael Edwards, for example, said, "My daughter came with me, who is a nurse, and she had a lot of good questions, that's why I brought her." Another participant, Leonora Smith, stated:

> I didn't have the vaguest idea of what to ask. I mean, you just come in like a dummy, you know. You really don't. M. [her friend] did most of the asking. She wrote questions down on a sheet of paper and she had more questions....I may have passed that test [Mini-Mental State] (laughs) I wasn't thinking too clearly in the beginning.

It would appear that this woman knew that her own anxiety

would get in the way of full comprehension and so she used an appropriate strategy to make sure that she reached an understanding of the trial. Similarly, other participants stated that family members or friends who were members of the medical profession were "more qualified" to ask questions.

There were some participants who spent a great deal of time with the protocol and informed consent document before deciding to participate. Margaret Gross, for example, a woman with breast cancer who was extremely knowledgeable about her treatment, stated:

> He [the investigator] gave me a 40-...or 50-page copy of the trial. I proceeded to go to Kinko and made seven copies and made an appointment to see [her oncologist] two days later and sent a copy of it to [another oncologist], my doctor...and an attorney friend of mine who's been through some trials to read for efficacy, and another doctor friend of mine who's had a bone marrow transplant to go through and see if there's a weak thing I didn't pick up.

Similarly, Carol Spicer, a 46-year-old woman with recurrent melanoma described reading the protocol in this way:

> Well...my neighbor friend, who's my best friend, and I sat one afternoon and we spent two or three hours going line by line and discussing what

every line meant, and we wrote all the questions on the outside, the things that we didn't understand. And I came back and Dr. W. spent time with me and answered all my questions, and then I signed it.

This participant felt that after this process she had a clear understanding of the trial before she agreed to participate. She put it this way, "I feel that I signed the true informed consent. Yes, I know exactly, exactly what's going on."

This concentrated effort and attention to detail that participants demonstrated clearly reflected their determination to choose the best available care for themselves. It also reflected their commitment to retaining their own autonomy in decision making with regards to their treatment.

Two of the participants also suggested that it would be nice to be able to talk to other patients who were enrolled in the same trial. Jane Martin expressed this desire:

> I think if they could have put me in touch with someone who had already started the program where I could say to them, "What's it like? Does it hurt? How do you feel?" You know, whatever, just to know what to expect. I mean, they tell you on paper what they're going to do to you but

you don't know what that always means.

Although Ms. Martin read and understood the consent form, she wanted information specifically about what she would experience while on the study.

Although most participants were eager for treatment, they did appear to consider toxicity issues in the decision process. Thomas Williams, for example, described the way in which he approached the trial this way:

> They gave me a list of side effects that they noticed in rats. It hasn't been tried on humans...There's no information available on it...they said it was really excessive doses, also. You expect some. None of the things that they said were really that bad. I wouldn't want to stop it.

Steve Powell, a man with advanced lung cancer also was anxious for treatment but looked at toxicity as well. He stated he would take the treatment, "Just as long as I ain't gonna drop dead from not the cancer but from the treatment, you know." Edward Cortez, another man with advanced lung cancer, did have some significant neuropathy from his treatment, but he was philosophical about the side effects:

> You know, you, when you taking like chemo and things like this, you have to expect some side effects. You [know], if everything be roses, it

be beautiful. So you gotta expect something. Be nice if it can cure you, no pain whatsoever. You know?

On the other hand, Willard Holmes, after an 18-year battle with melanoma and several clinical trials, had this to say, "At this point, I'd say I feel less strong about doing just anything. Especially if it has side effects." Another participant, Shirley Palmer, described an active search for treatment after her colon cancer had metastasized to her liver and lungs, but also stated that she would not take anything that came along:

> Well, I don't know I'd take "anything," but we would certainly look at it and run it by to see what it is....I guess probably we would want to look at any earlier patients that were on it and the side effects and that kind of thing. You anticipate side effects in any of this.

In contrast to the majority of participants, a few did not read the written protocol information and informed consent carefully, for they had already made up their minds to take whatever was offered. Thus, Thomas Williams related, "I read it. I had pretty well made up my mind before I came in. I wouldn't have bothered with it if I - You're in for it or you're ....You go for it." Steve Powell, a 50-year-old man with advanced lung cancer, read the protocol and had his friend read it, but signed the

consent right away because as he said, "I don't know about chemo. All I know is people die from lung cancers. I don't really have any options, choices."

Some participants, then, were so eager for treatment that they spent very little time in the decision process. In contrast, most participants, although they had actively sought the clinical trials for which they were being considered, carefully reviewed the study information and discussed it with others before consenting. Participants also universally considered potential side effects when making their decision.

Hope

Participants actively sought treatment and all agreed to participate in Phase I clinical trials. They did so because these treatments provided hope to cancer patients who had few or no other options.

Participants understood the risks and benefits of the Phase I trials in which they participated and they stated they understood that there were no guarantees and that they might not benefit from the treatment, but they held on to the hope that they would benefit. Although only two of these participants showed an objective response to their investigative treatment (see Table 3), every one of them had positive expectations from the treatment; all hoped for benefit.

Participants had many expectations of benefit from the

Phase I clinical trials. Among the hopes participants expressed were: (a) to extend their lives, often in order to accomplish some task; (b) not to die from their cancer; and (c) to be cured or at least see some improvement in their disease. Some participants, recognizing that they had no other options, stated simply that the trial gave them hope and were not specific about the hoped-for outcome.

Extension of life. One of the outcomes hoped for by participants was an extension of their lives. Many talked of their desire to "buy time" to finish certain tasks or even to allow new treatments to come on the scene. Mabel Scott put it this way, "It's given me more time to do some things and get some business settled that I wanted to do. Like I wanted to sell my home, and rather than leavin' all that for my kids to do." Ed Woodward had a specific reason to hope for more time: "We have, my wife has two boys. We have one, like I say, in grad school. He's getting married in June. I, obviously would like to be there." This participant died before a second interview could be scheduled, but he did live long enough to attend his son's wedding.

Beatrice Howard, a 60-year-old woman with melanoma, simply stated, "I'd like to get better and live a little longer." In the same vein, Michael Edwards gave this reason for choosing a Phase I trial: "So I can be around a

little while longer, 'cause I want to enjoy my grandchildren, and all of the rest of my family, of course, includin' my wife and everyone." Finally, Margaret Gross specifically hoped to buy time until another treatment came along, as she stated, "Based on the fact that I know I'm going to lose my hair and all have side effects but basically if it gives me another year or two, there's something else out there." Her statement reflected the common belief that effective treatment is "out there" just waiting to be discovered.

Not to die. Some participants hoped, simply, not to die. An example is found in this excerpt from an interview with Laura Thompson, a 58-year-old woman with advanced lung cancer:

CM: Was there any one thing that made up your mind that you should go ahead?

Laura: (Nods)

CM: What was that?

Laura: I want to live.

Similarly, as May Hogan described her initial diagnosis with breast cancer, she had this to say, "And instantly, 'I want to live' came to my mind, just that quickly, that I wanted to be here." Margaret Gross also, when describing her quest for more treatment options, stated, "I'm determined not to die of this thing."

Cure or improvement. Other participants expressed

hope, specifically, for an improvement in their disease, even a cure. Mary Hogan had specific outcomes that she hoped for. "I was hoping I would feel better, I was hoping to go into remission. I was hoping to get rid of the back pain, I guess I was hoping to feel better." Michael Edwards put it this way, "There is no guarantee, but it's something to give you hope, that, hopefully, it'll cure the cancer." Leonora Smith also understood that the treatment might not work. She said, "Well, of course, I was hoping it could make it all go away and I don't know but maybe they can." Sharon Barnes cautiously expressed her hope that her melanoma would respond by saying:

> I'm hoping this will help. I, you know, I really because of everything I've read on it and everything, I would be shocked, I would be very amazed if it never came back again. It would be wonderful. But I would be happy if it just prolonged it.

Similarly, Mark Stewart stated, "Well, of course, you know, I hope for a reduction in the size of my tumor, but after eleven years of doing so many different things, anything positive will make me happy."

Nonspecific hope. Some participants were less specific, stating just that they had enrolled in the trial because it offered some hope. For example, Thomas Williams said, "When we came back in and spoke to Dr. R. we decided

to sign up right now for it. 'Cause at least there's some hope there." And Carol Spicer said, "Now I feel like I have a hope." Edward Cortez described his physician's assurance that his cancer would go into remission then remarked, "So he give me a little hope. Good doctor."

Hope, then was something these participants held on to. Mary Hogan was clear about this need: "I've only asked two things, one is, don't give me a life expectancy, and don't tell me if it's life threatening. So nobody has scared me. They don't take my hope away."

That the Phase I trial offered participants some hope is evident in their frequent statements that there was nothing else for them. Many felt that if they wanted a chance at all they had no choice but to enroll. Steve Powell expressed it colorfully, "But you don't - looking at - just boiling it down to what it is, you really don't have a lot to - die, you know. Where's your decision, you know. What're you gonna say?" And Mark Stevens, when asked his main motivation for going on a Phase I trial, replied, "There was nothing else." Again, in his second interview, Edward Cortez, a 62-year-old man with lung cancer, was talking about his options after being taken off study. In discussing the possibility of going on another investigational protocol, he had this to say:

> Because if the tumor is, for example, is not completely gone...and start growing again, so

then...might as well take the other one, because otherwise it's an only short time, then it's going to take me away from here, the tumor. It's gonna grow so big that it's gonna choke me to death.

Perhaps because they perceived no other options, participants sometimes found a way to understand their chances of benefit to be more than they had been told. Margaret Gross, for example, although she stated in her interview, "I know that most, like 95% of trials, Phase I trials fail," nevertheless also made this statement:

> He explained the trial to me and I immediately understood that it was so non-invasive compared to any of the high-dose chemos I had been on, and my understanding of the trial was that I, to me I had a 300% chance of reacting versus a maybe 3% chance of reacting on chemo.

In the same way, Carol Spicer described her understanding of the chances of benefit:

> And I feel fortunate in that even, you know, I think it's gonna work, because...we went into the statistics of the thing and found out more, like the demographics of the people that have had good results and they fall into my category, so that makes me more hopeful, you know, plus I know, I've done research and I know what my chances

would be with wicked, wicked chemotherapy.

It is interesting to note that patients on biotherapy protocols universally described their perceptions that this treatment was better than chemotherapy. This perception may be based on its being a relatively new approach or on its being less toxic, typically, than chemotherapy.

Living on a Trial

After participants had decided to participate in a Phase I clinical trial, the next step was living on the trial. Issues of quality of life became more important to them, and they also sought to find meaning in their participation in the research process.

Quality of Life

As was evident in their discussion about toxicities, participants in Phase I trials were concerned about their quality of life. Thomas Williams, who had been told that no treatment was available to him and that he should go home and enjoy the rest of his life, later enrolled in a Phase I clinical trial. He said of possible toxicity: "That would have, that would have been one of the things that would have changed my mind. Because I've still got the thing about enjoy the rest of your life." Another participant, Ted Church, a 75-year-old man with prostate cancer, said, "I've always felt that living is fine, but the way you live or, how should I say, the...how you live, the, the quality of life."

Physical. In general, however, participants on study described their quality of life as good to excellent. Several mentioned treatment-related improvement in their symptoms as contributing to an improved quality of life. Margaret Gross, for example, stated that her quality of life was better while she was on the study because her pain had lessened. Mary Hogan, another woman with breast cancer also mentioned that she felt better, saying, "Basically, I feel a whole lot better, I'm more interested in doing things whereas before I was just, I was basically in bed getting weak, weak." Leonora Smith reported little change in her quality of life since enrolling in the trial: "I don't think the quality of my life has changed so much. I get tired. I have, you know, days when I don't care whether things keep or not, but not, not really bad."

Like Ms. Smith, the majority of participants experienced fatigue related to treatment and for some, it was debilitating. In fact, more participants reported fatigue than pain, with 14/20 participants identifying fatigue as a problem for them and only 2 identifying pain. Fatigue seemed to have a more profound impact on their quality of life. For example, Christine Braun, when asked about her quality of life, said, "I still will do what I used to do, but, you know, the thing is, sometimes I get more tired." Sharon Barnes also described fatigue from the treatment: "I did feel, uh, I just feel tired. I felt

tired, just not myself." Finally, Steve Powell described his fatigue this way:

> Well, it's just all the time. Continuously. You know I'll go home and they'll say, somebody'll call and says, "Why don't you come back?" I go, "I'm tired." I just sleep a lot. You know, relax. So I'm not workin', I'm not doing anything right now. I'm just trying to fight and beat this cancer - it seems like I'm doing it, but it's the fatigue. I don't basically do anything all day.

Physically, then, participants felt generally well but had to contend with fatigue which interfered with their being able to do everything that they wished.

Social. As with Steve Powell, the fatigue and other symptoms affected the social domain of participants' quality of life as well. For example, Ed Woodward said:

> You know with friends, we're trying to maintain our same life style that we've always had, cut back a little bit, we don't go away on, you know, three week vacations or anything like that but even just go to the theater or something like that, we try to keep the same schedule as what we normally do and, and I say to myself, tonight, even though you don't feel like going, why don't we go out, you know, and that's so, mainly from

the fatigue standpoint, you worry that, you know, you may [not] have enough energy.

Albert Paredes also talked about his limitations, saying:

> Well, I'm reduced quite a bit physically. I mean, I'm, I wasn't doing a whole bunch physical but I do a lot of the work around my house, to my cars, we go to the desert with, I don't know if you're familiar with the dune buggies and the sand rails and all that stuff and it becomes a lot of work just to pack all that stuff up and go and do all that stuff and I have to have my son do a lot of the work.

Psychological. In addition to the physical and social domains, quality of life is postulated to involve psychological or emotional well-being. Few participants reported on this aspect of quality of life directly, although Jane Martin did say that participating in the trial had removed her anxiety about not doing something to treat her disease. She said, "Part of me has some peace in that I'm doing something." The hope that is generated by clinical trials may also make an important contribution to quality of life (Rustøen, 1995).

Spiritual. Another aspect of quality of life mentioned by a few of the participants was the spiritual. One participant, in her second interview, told of seeing a vision of a prophet while undergoing an MRI scan. She felt

that he had come to her to give her hope. Since that experience, she has returned to her faith, and she says, "I think the real cancer survivors have a real deep soul enrichment that they never had before, and I went back and found myself a temple and a rabbi, and a cantor and, and it's...wonderful." Other participants mentioned prayer as a comfort. In his second interview, Michael Edwards mentioned his strong Catholic faith and said,

> Believin', you know, that, that even if I were to get sick again whatever, I think that God is going to help me through it one way or another, so I think that, my faith in God has a lot to do with it. And also my wife and family and all those, their prayers and all really helped a lot.

Even participants who were not affiliated with a particular religion talked about a strong faith as sustaining them, especially as they had to contemplate their own eventual deaths. For example, Leonora Smith, confided that she had never been baptized although she had been raised with a Protestant faith. Now that her lung cancer was advanced, she wished to be baptized. Baptism became important to her as she reached the end of her life.

In addition to the side effects of treatment, other aspects of participating in a clinical trial can affect the participant's quality of life. Two of the burdens identified by participants were transportation issues and

having to wait for long periods of time in the clinics.

Phase I clinical trials are not available at every hospital. Generally, only comprehensive cancer centers conduct Phase I trials and each center has specific trials. For some participants, then, participating in a Phase I trial meant traveling across the country, as the Martins did. Asked about burdens to her participation in the trial, Jane Martin said, "Flying out here. And the cost." Travel for participants from out of state involved the expense of plane fares, even when there was limited assistance from organizations such as the Corporate Angel Network. For some, travel expenses were a major factor in their deciding whether or not to participate in a given clinical trial.

Even for participants in the local area, transportation could be a problem. Ed Woodward was able to have one of his sons drive him to the clinic, but he noted:

> It would have been a hassle, and I'm also somewhat concerned with my wife driving that distance as she's diabetic and she has vision problems. I wouldn't feel good. Normally when we're together I always drive and I think I can still but I didn't know what my reaction would be to the medication whether I would be able to drive.

Mabel Scott, who traveled approximately 80 miles one way,

also depended upon her children for transportation. She said,

> I had to depend on children and I was told that I should be there every 28 days so it was a little difficult to find, out of three daughters, somebody that could take a...day off to get me there - that was one of the biggest problems.

Albert Paredes also found the drive to be a burden. He related:

> Well, we've, we've in the last couple of days haven't spent much time at home. We've got a...uh, a 40, 50 minute drive on the freeway depending on traffic and like tonight, we won't get home until 8:00 o'clock, probably.

Finally, Edward Cortez relied on public transportation, taking a commuter train and a bus. It took him an hour's travel time each way, but he stated that this was not difficult for him.

Another burden frequently mentioned by participants was having to wait for extended periods of time in the clinic. Mark Stewart complained of having to wait and "inconvenience other people." He said,

> When the treatment takes five minutes, and you're still - you know, you're here for three hours just waiting for the lab results so you can have the treatment, and then you have to wait hours

afterwards so they can observe you.

Mr. Steward stated that the time involved in waiting was the biggest burden of being on a trial. Another participant changed from one major cancer center to another, in part because of having to wait up to an hour and a half at each appointment.

Side effects of treatment affected quality of life for the participants as they do for all cancer patients. In addition, the burden of transportation and waiting for observation affected quality of life. Because clinical trials are conducted at only a few centers and rely on observational data, these last two influences may be more pronounced for participants in clinical trials than for other cancer patients.

Participants chose clinical trials primarily because they wanted treatment. They were also aware, to a great extent, of the research purpose of the trials, and they sought to find meaning in their participation.

Meaning

Participants indicated that their primary motivation for participating in a Phase I trial was the hope of benefit themselves, but they also talked about benefitting other patients "down the line" by their participation. In fact 15 of the 20 participants gave "helping others" as one reason to participate in the trial. Beatrice Howard, for example, said, "Uh, I feel that it's something that

possibly might help me, and if it doesn't it might help somebody else down the line." Similarly, Laura Thompson described deciding to participate in a Phase I trial: "They asked me if I was interested and I said sure. It might help somebody in the future." Carol Spicer also stated, "I think one of the big things is that I hope that what I'm going through helps somebody else, you know."

Helping others was a way that participants had of finding meaning, a way of knowing at the end of their lives that they had made a difference. Christine Braun, for example, said, "After all, you can't just go on forever and maybe this experience will help someone else." Sharon Barnes, in this excerpt from her interview, had almost the same thing to say:

> CM: Do you feel - do you have any particular feelings about being part of a clinical trial? Scientific research?
>
> Sharon: Actually, I'm glad to do that. I would do it again. I would do it to help someone else.
>
> CM: Okay.
>
> Sharon: More or less than myself. If I can do something to help someone else, I mean, I kind of think my life is, you know I haven't had children, my husband died, and so I can't do much to change my life at this point, but maybe we can help somebody else.

It is striking that Ms. Barnes mentioned not having had children as a factor in her wanting to help others. It is as though this act is her legacy to future generations. Summing up her feelings about participation in the trial, Carol Spicer said this: "You know, it's funny, I don't know, I, it gives you a reason, you know. I mean, it makes you feel important."

Participants who had children often mentioned them as a reason for their willingness to enroll in a trial - the children might benefit in the future from the research. Mabel Scott, an older woman with ovarian cancer, when told by her physician that the trial might not benefit her personally, had this to say, "But you must remember that I have sisters and daughters, and if they happen to come out with something like this, maybe something that I have done would be beneficial to them." Michael Edwards also stated, "It's, what I sayin', it's not necessarily for me, but...my children and grandchildren down the line, 'cause I have five children and nine grandchildren." And, again, Jane Martin gave this account:

> I hope I will get some benefit from it, but, in the long run, I mean, obviously, I'll be helping other patients. We don't know if this was hereditary or not. I have a daughter. I'm hoping they will find a cure for this. And if this, if it comes from this, whether it's for my

daughter or for somebody else, you know, it would make me feel very good to know that I helped them, yeah.

Participants also demonstrated appreciation for the research purposes of the trials they were on when they spoke of contributing to the research effort and making sure that they did not compromise that effort. Leonora Smith said, "I know that, that lung cancer is not considered curable. But whatever the progress they make I'm willing to be there to help the progress be made." She also related that she had suffered pain in her legs but was afraid to take anything for it, saying, "I didn't take anything because I had no ibu-, I had ibuprofen but I hadn't asked if I could take it and I kept thinking, well, that's going to ruin the study if I'm not supposed to have it." Another participant, Margaret Gross, talked about some Chinese herbs that she was taking, saying she wouldn't take them until she had first shown them to her physician for approval. She said, "I didn't want to compromise the study, because if he said, 'No,' I wouldn't take them." Finally, Carol Spicer told of her desire to adhere to the study because she felt that the treatment she was on was a real breakthrough. She said:

I think this is it. I'm convinced. I really do. And that's one of the reasons why I keep - I do everything he tells me to do. If he tells me to

be at point A at 11:00 o'clock, I'm there. I don't mess up, and I don't bitch and moan, I just do it because I really think that this works.

Other participants stated that they understood that goals of both research and treatment were important. Thomas Willard, for example, said:

I don't want to try to sound noble or anything, like I'm doin' this for the advancement of science. That's part of it. That's a by-product so far as I'm concerned. Of course, from the other side of the coin, so far as they're concerned if they help me, that's a by-product. They're looking to advance sciences.

Albert Paredes expressed a similar thought when he said, "Yeah. I mean, it's a two way street. I'm, I'm hoping for a result and so are they, so...I need them. They need me."

Although some participants felt that both the goals of research and the goals of treatment could be reached, at times the tension between the two was evident. Willard Holmes, for example, participated in a Phase I biotherapy trial and believed that he got benefit from it but was taken off due to disease progression. He tells the following story:

So, so then I did two, two treatments of the [biotherapy] and I got a, I can't remember if it was a CAT scan, or what, I got some kind of, did

some kind of test to see how we were doing and the disease appeared to be progressing. So...but I was feeling better. And the doctor said, you know, that, he said he couldn't keep me on, he couldn't keep me on a protocol unless he could prove that it was showing, that it was working. That, you know, the FDA would take his license away. I didn't really want to stop the treatment because I was physically feeling better and, by golly, something was working.

At his second interview, he was still convinced that this treatment was working for him and he had this to say:

The only thing I'd like to say, and I feel very strongly about this. Is that I think there should be some part of the mechanism whereby if someone does do a protocol, and it does help them, there should be a way for them to follow up with first treatment. The fact that I can't get [the biotherapy], I think is disgraceful. I mean, it's just, I can't think of a strong enough word to say. I don't even want to get going, it makes me so angry. I mean, there's something exists that works for me and I can't have it.

Another participant, Thomas Williams, also felt that he should not have been taken off his study:

And even after they took me off it at first, I

> wasn't convinced that that was the right thing to do....I felt that they were going to - I thought maybe they had taken me off too quick because I was the first, and I had the lowest dosage you know, maybe a increase in dosage would have allowed this to work better.

Here, he expressed his clear understanding of the dose escalation that takes place in a typical Phase I trial. Other participants expressed their desire to stay on their current treatment as long as possible, since they felt that they were benefitting from it.

Participants, then, saw their trials as treatment first and research second. They were, however, all aware that they were subjects in an experiment. Some stated that they felt like guinea pigs, while others rejected that term. Christine Braun said, "Well, you know you're a guinea pig, but what you get might help you or it might help someone else, and I think it's a good thing because I get the newest thing." Michael Edwards also used the term "guinea pig." He said, "I had other people tell me when I was in this thing, 'Oh, don't let them make you a guinea pig,' and I said, 'How do you not (laughs) make me a guinea pig?'" And Albert Paredes noted:

> I feel exactly like a lab rat. Give me a little wheel and I'll chase ...whatever they chase. There's no question to that....It's a different

> ball game. You've got drugs where they, they're established and the doctors look at your cancer, look at you x-ray and they pretty much know what to expect or what not to expect, and you jump in the research arena and ha ha, you know, they're on you, they're asking you questions and they want to know what is happening to you.

On the other hand, Mary Hogan said that she and another participant called themselves "pioneers." She also noted, "I've always been interested in a clinical trial because I've always felt like people preceded me in making the medicines that I use, and when I started in '90, there was no Neupogen and there was no Zofran." Thus, this participant saw her role as a research subject as one in which she is blazing the way for future patients.

Although participants sought out Phase I clinical trials because they wanted any treatment that would offer them hope of benefit, they also understood that the trial was research and the treatment investigational. They tried to preserve the integrity of the experiment because they felt that the findings might improve cancer care for future patients. Some were convinced they were on the leading edge of cancer treatment. Other participants expressed the belief that both they and the research could benefit from their participation.

Dealing with Uncertainty

Eleven of the twenty participants were able to give a second interview. At the time of the second interview, only two of the participants were still enrolled in a study. About half were receiving standard treatment of some kind, the rest were receiving no treatment at that time. Characteristic of the second interviews was a focus less on the trial itself and more on the uncertainty inherent in living with advanced cancer. In fact, ten of the eleven participants who gave second interviews talked about not knowing what the future held. Christine Braun expressed it this way:

> In the back of my mind, I'm thinking that someday it will kill me, you know, but you don't know when, and, and in a way it is good that you don't know, but on the other hand, it is not good either, you know you have it, you cannot relax with it. You know, when you can't sleep at night, you lie in bed and you toss and you turn and you think, God, what will be next year, and, you know, you keep thinking.

For Jane Martin, the uncertainty was centered on her follow-up examinations:

> I'm fine 'til about a week before and then it starts building...It's like, you know, I want to go to him and say, "Don't look and don't feel," you know, "Don't do anything else." So it is

very stressful. Until I hear the words, (clears throat) until I hear the words, you know, "I don't see anything. Everything looks good. Everything feels good." And then we breathe a sign of relief, but it's very stressful.

Margaret Gross also talked about the uncertainty and frustration related to the possibility of a recurrence. She said, "Always knowing, you know, you, you deal with when's it gonna reoccur? It's always with you, okay, and that, how do you, you know, that anger, okay? It's a daily thing."

These participants talked about the stress inherent in their awareness of having a life-threatening disease. They described the difficulty of planning activities when they couldn't be sure that they would be well enough to carry them out. They also talked about the necessity of going on with their lives despite this uncertainty. A common strategy was described as "not dwelling" on their disease. Mabel Scott, for example, said this:

> I think I'll be better off if I go along day [by day] and not think, "Oh, I've got ovarian cancer, I'm dyin'." Instead I think, I've got to get something done to these curtains so it'll be clean in here. I would rather do, live that way than worry about myself.

Another participant, Michael Edwards, said, "I really don't

think about it a whole lot. I guess I'm too busy with working away still, which I probably will be working away the rest of my life." Ted Church also noted, "Meanwhile, I tried to carry on a normal way of life." Carol Spicer found her work a welcome distraction. She said, "You know what's nice about working, like being able to work when you're on program, I don't even think about it."

Finally, some participants spoke of the intrusive quality of their awareness of their disease. Leonora Smith said,

> You know, since this began and I don't know, you try to avoid - what else is there to do? It's there. You're part of it, so why dwell on it. So just take care of it. It follows you around no matter where you go or how hard you run.

Christine Braun also expressed a similar feeling:

> You know there is something and you, you feel something and you think, "God, I wonder what that is now," you know. If you can just put it aside and just to go on, but there it is always around, you know.

Participants felt that they had good quality of life when they were able to carry out their usual activities and when they could do the things they wanted to do. For some, carrying out normal activities involved ignoring the presence of their cancer. This was something that

participants were more than willing to do. Carrying out normal activities meant that they were still part of the world, still truly alive, or, as Laura Thompson said, "You don't feel so lost like, you know. Like, I'm going to die."

Summary: The Quest for Treatment

For cancer patients, the decision to participate in a clinical trial began with the decision to seek a clinical trial. When patients discovered that there was no standard treatment available to them, they often decided to seek other options on their own, including clinical trials. The quest for treatment was an active search process in which participants described using all the resources available to them. These included the Internet, the National Cancer Institute hotline 1-800-4-CANCER, television and radio programs, personal and family connections, and networking with other patients in clinics and support groups.

For these participants, treatment on a clinical trial represented the hope of improvement in their disease, the hope of extending the time left to them, and even the possibility of cure. It also represent the chance to do something to help themselves, rather than to do nothing and accept the inevitable progression of their disease.

The participants were open to clinical trials because they felt that they had few if any other treatment options. Many have stated that they felt they had no other choice.

However, the decision to enter a trial was not automatic. Most participants not only read the protocol and discussed it with colleagues and family members, they asked questions and insisted on candid answers. Many also stated that if the anticipated toxicities were too great, they would refuse the trial because quality of life was still important to them.

Indeed, most participants defined their quality of life while on study as good to excellent, stating that they felt physically better on treatment and that they also took emotional comfort in knowing that they were doing something to help themselves.

In addition to the hope of personal benefit that accompanied a clinical trial for most participants, there was a need to contribute to the research process in the hope of benefitting future patients, possibly their own children or grandchildren. This was expressed in their statements that, while their own benefit was their primary motivation for participating, they also considered the potential benefit to others. In fact, participants have stated that they followed their physician's directions to the letter so as not to compromise the study. Several participants also expressed the hope that their interviews would help other patients down the line.

Chapter 7: Discussion

Review of Findings

The participants in this study provided insights into the experience of participating in a Phase I clinical trial from their own perspective. Through the analysis of data, common elements in that experience were identified; these elements were described as essential categories and themes. Although some of the findings of this study support those of previous investigators, other themes have not been previously identified.

Much has been written about the ethical issues involved in recruiting cancer patients to Phase I clinical trials. Certainly, those patients who qualify for Phase I trials are among the most vulnerable. They must have no other therapeutic options open to them. Often, these patients have advanced disease and may even be terminally ill. To subject them to the risks inherent in the first human studies of a drug primarily for the purpose of assessing that drug's toxicity, raises many ethical issues (Emanuel, 1995; Lipsett, 1982). Physicians often shy away from referring patients for Phase I trials because of these issues. However, the data indicate these 20 patients expressed their need to participate in these trials for their own reasons. Participants in this study spent hours on the Internet and traveled thousands of miles in order to enroll in a study that offered some degree of hope to them.

These findings present a very different picture from the one presented in the literature. The findings suggest that cancer patients may seek clinical trials with full knowledge of the research involved and desire the opportunity to participate in them, not in spite of but because of their understanding of them.

The Quest for Treatment that leads some patients to seek out clinical trials has not been previously identified in the literature. In the study by Rodenhuis et al. (1984), for example, all the participants were recruited to Phase I trials by their physicians. Yoder and her group (1997), stated that half of the patients they interviewed had been informed of the trial by a physician. In another study, Daugherty et al. (1995) interviewed only those patients who had already signed a consent to participate in a Phase I trial but did not explore the ways in which patients came to the trials. They did note, however, that a total of 75% of their patients listed a physician as the most important person with whom they discussed their decision to participate.

Even more striking, Cox and Avis (1996) in their study with seven patients on Phase I trials in England, found that "all patients involved in this study described the doctor as being the one who made the overall decision about their treatment and believed that the doctor was the best person to decide what was right for them" (p. 181). These

findings are in sharp contrast to those of this study in which patients reported challenging their physicians' advice and sometimes rejecting it outright. Their decision to participate was based on their own understanding of the risks and benefits after consultation with friends, family, and other health care professionals.

The participants in this study demonstrated an independence in seeking treatment that has not previously been recognized. As a group, they expressed themselves as spirited, opinionated, determined, and self-directed. Rather than allow their physicians to make treatment decisions for them, they took charge and proactively sought their own trials, using the physician as one of many resources. They also demonstrated thoughtful consideration of the options presented to them.

The participants in this study were generally well-educated, articulate and reasonably affluent. The question arises, then, of whether this theme of an active quest for treatment holds across demographic differences. Seventeen of the 20 participants had attended college, and the majority of those who would disclose their income earned more than $60,000 a year. It is possible that those lower on the socio-economic scale were less sophisticated, less proactive in their search for treatment. Half of those with incomes under $30,000 were referred to their study by a physician, and the three participants who were being

treated at a public rather than a private hospital had all been referred by a physician. This finding was in contrast to the majority of participants, who had obtained information about the trial through their own efforts. However, the sample size in this study was too small to draw any conclusions related to socio-economic differences. Also, even the less affluent patients expressed an interest in their own care, to the point of using any resources available to them to obtain information. Steve Powell, a 50-year-old man with lung cancer, describes how, after his diagnosis, he was referred to a public facility and told that it was one of the best cancer hospitals in the area. Not content with that recommendation, Mr. Powell "double checked" by asking others and also looked into an alternative therapy that he had learned of through talking with another patient in the emergency room. He also stated that he keeps informed about the newest cancer treatments by watching television news programs and by talking with friends and acquaintances.

Another question is, at what point in the disease trajectory do patients decide to take charge of their own treatment? It is likely that patients become more sophisticated in their knowledge of cancer treatment and the resources available to them over time.

The availability of information on the Internet is a recent development that enables cancer patients to seek and

find the newest treatments and the most promising clinical trials. Iwamoto and Hockenberry-Eaton (1995) published a case study in their "Multidisciplinary Rounds" department in Cancer Practice that was entitled "Protocol 'shopping' on the Internet." In this article, physicians, nurses, and social workers were invited to comment on the problem of a patient who spends her time searching the Internet for protocols to treat her multiple myeloma and insists on directing her own treatment. This patient was recognized by some as part of "a new generation of oncology 'consumers' who take an active role in treatment decision making" (p. 275). However, other contributors suggested she needed limit setting and to be encouraged to "allow the physician to guide her throughout the continuum of her care" (p. 277). Finally, it was noted that "the ease of public access to information that was previously available almost solely to health professionals has presented a challenge to cancer care providers" (p. 277). Health professionals are increasingly challenged by the active roles that patients play in demanding participation in decision-making. In addition, patients may find treatment options that are unknown to their physicians. Certainly, the sample in the current study was proactive and independent in their approach to treatment. Detailed treatment information is available on the Internet or through the Cancer Information Service to all patients.

Therefore, health care professionals need to access this information themselves and review it for appropriateness and accuracy so as to be able to offer greater support and guidance in treatment decisions (Liebman, 1998).

Informed consent is another issue addressed in the literature. There are two concerns about informed consent for Phase I clinical trials: (a) whether the potential benefits to the patients outweigh the risks involved and (b) whether this vulnerable population can give a true informed consent (Emanuel, 1995; Lipsett, 1982; Markman, 1986). This study supports the findings of Daugherty et al. (1995) that participants feel they make the decision to participate in clinical trials autonomously and that they have an adequate understanding of the trial, based on the information given them. In the study by Daugherty et al., however, most patients were unable to state the purpose of the trial as one of dose determination. In the present study, this question was not directly asked, but as has been seen, all the participants were aware that they were participating in a research study and a few commented on the nature of a Phase I trial with these observations: "They're testing for dosage"; "This is just [a] toxicity study still"; "It's a dose escalating study to find out which doses are safe for people to tolerate"; and "They're not testing how it works, they're testing toxicity." Two were sophisticated enough to realize that, as early

participants, they had been given a lower dose than later participants and so had a lower likelihood of responding. Thus, these participants seem to have been well informed about the nature of Phase I trials.

Does the potential benefit to these patients outweigh the risks involved in the trials? Phase I trials are conducted to establish dosage and toxicity. However, there is always therapeutic intent (American Society of Clinical Oncology, 1997) and patients as well as investigators hope for tumor response from them. It has been suggested that, because objective response rates are so low, benefits to patients are too low to justify the risks involved. While it is true that response rates are low generally and were low for this group of participants as well, the participants were aware of the likelihood of response and still felt motivated to "take a chance." Or, as one participant put it, "You have to take the risk, you know, you have to do and see what you accomplish."

The motivations that previous studies had identified for patients participating in Phase I clinical trials were supported by the findings in this study. Patients were strongly motivated by the hope of benefit and by the knowledge that no other treatment was available to them. However, the possibility of benefitting others was also a significant factor in this group of patients. Both Daugherty et al. (1995) and Yoder et al. (1997) found that

the primary motivation for entering trials was the hope of benefit and discounted altruistic motives. In this sample, however, while hope remained the primary motivating factor, 75% of the participants interviewed mentioned "helping others" as an important consideration. It appears that patients are seeking out clinical trials as the only available treatment option, one that at least gives them some hope, but that they also seek to find meaning in their participation and that this meaning involves consideration of the benefit to future patients.

The Quest for Treatment, in which participants took an active role in seeking treatment, decided to participate in Phase I trials, and learned to live with the burdens of the trial and the uncertainty of their conditions, followed a definite trajectory for most participants. This trajectory is consistent with Stetz's (1993) findings about "survival work." In her conceptualization, patients and their spouses began by engaging in survival work and gathering information related to the decision to enter investigational treatment. This phase corresponds to the steps of Taking Charge and Deciding. Monitoring was the phase related to the actual treatment time, the step identified here as Living on a Trial. Finally, she described Carrying On as the phase that began when the patient realized that the treatment would not control the cancer. This phase corresponds with the step of Dealing

with Uncertainty. During the phase of Carrying On, participants were involved primarily with getting on with their lives. They, like the participants in the present study, tried to carry on with normal activities in the face of an uncertain future. The close correspondence between Stetz's (1993) findings and those presented here lends credence to the categories and themes identified as essential to this experience.

Throughout the course of the Quest, quality of life emerged as an important consideration for these participants. Not only did they consider quality of life issues when deciding whether or not to accept the Phase I trials offered to them, but they talked about the effect of their participation on their quality of life. The findings from this study are consistent with the concept of quality of life as subjective, multidimensional, and dynamic (Cella, 1994; King et al., 1997).

Quality of life for these participants changed with changing circumstances. Side effects of treatment were an important consideration for them. Fatigue, especially, interfered with quality of life for it prevented participants from carrying out normal life activities. However, the hope engendered by the trial and the peace of mind of knowing that they were doing something to help themselves improved quality of life. Uncertainty, related to disease recurrence or progression, diminished it.

Other aspects of being on a Phase I clinical trial also had an impact on participants' quality of life. Transportation and logistical problems added to the burden of the trial as did the long periods of time spent waiting in the clinical areas. In a recent article in Cancer Practice, Guidry, Aday, Zhang, and Winn (1997) also found that transportation could be a barrier to cancer treatment. In their study, access to even conventional treatment was limited for some patients, especially minority patients, because of transportation difficulties. They suggested that their study "points to the need for healthcare facilities to facilitate the provision of transportation assistance for patients with cancer" (p. 366). The problem is that much greater for participants in Phase I trials, who must often travel great distances for treatment.

Limitations

This study was a preliminary inquiry into the experience that cancer patients have on Phase I clinical trials. It resulted in a complete description of their experience, but is not generalizable in the sense of being representative of all patients on Phase I trials. The study was limited by including participants from only one geographical area and primarily from an upper socio-economic class. It was further limited by having research nurses select the participants, because they tended to select those who were articulate and cooperative.

Other limitations were inherent in the population studied. The underrepresentation of ethnic minority patients reflects the population of patients on Phase I trials at large cancer centers (Roberson, 1994). Also, the lack of Hispanic participants was related to the eligibility requirement that participants be fluent enough in English to be interviewed in that language. The difficulties of working with linguistic data in two languages prohibited the inclusion of participants who spoke only Spanish.

Even though these findings apply only to the participants studied, they do reflect conclusions reached by other studies of participants in Phase I clinical trials, such as those of Daugherty et al. (1995) and Stetz (1993). Also, this description of the experience of participating in Phase I clinical trials from the perspective of the patient may suggest possibilities and provide insights into that experience in other practice settings. Researchers and clinicians are invited to weigh the findings and determine whether or not the understanding gained from them is appropriate to their patient populations. Researchers are also invited to replicate these findings using other patient populations.

Implications

The findings from this study have implications for practice, education, research, and policy making. Insights

into the experience of patients participating in clinical trials can enhance clinical practice, suggest new research, and direct policy making related to clinical trials.

Practice

An important finding of this study is that patients seek out and eagerly enroll in Phase I clinical trials when they realize that there is no standard treatment available to them. They gather information from a variety of sources and take the initiative in determining their own treatment courses. Clinicians need to recognize the increasing amount of medical information available to the lay public and find ways to evaluate and support what their patients are learning. They also need to be prepared to engage in dialogue with their patients about treatment issues since fewer and fewer patients are content to follow their doctor's advice without question. This trend was reflected in the interviews with patients who challenged and even rejected the advice given them by their physicians.

Participants in this study related needing more information on what to expect when going on a Phase I trial; what it would be like and how it would affect their lives. The results of this study may be reassuring to patients deciding to participate in such a trial because most participants, while not realizing objective benefit in terms of their disease, nevertheless stated that they generally felt better both physically and emotionally when

they were on study. They also indicated that being a subject in a research study was not distressing to them but rather provided them with a sense of meaning at a time when their life might be drawing to a close. These findings may reassure investigators as well that patients are not unduly harmed by their participation in a trial that may benefit others more than themselves. The implication for clinicians is that methods must be found to enhance this sense of meaning in order to provide full benefit to these participants. For example, giving participants information about the findings of the study in which they are enrolled may increase their sense of meaning and the importance of their participation. Acknowledging them as "pioneers" in the development of cancer therapies may also enhance their benefit.

It is important to realize, however, that patients' quality of life will be affected by side effects of treatment and that fatigue is among the most distressing of these side effects. Fatigue prevents patients from doing things that they find pleasurable, an important aspect of quality of life. The cancer nursing literature is just starting to recognize fatigue as a major side effect in cancer therapy. Further study and the development of effective interventions in cancer-related fatigue are imperative.

Other treatment-related issues that affected patients'

quality of life were identified as transportation problems and waiting times. It may be necessary for cancer centers to begin to address transportation in a more consistent way. The American Cancer Society provides transportation for a limited number of patients; hospitals and treatment facilities might help to expand that program. It is also important that facilities address waiting times as a burden of treatment. Patients recognize that there will be occasional delays in treatment, but the time spent waiting is especially stressful for them, and every care should be taken to minimize that time. When waiting is unavoidable, such as when the patient undergoes a period of observation, means should be sought to decrease the associated anxiety. The provision of comfortable waiting areas, access to health care workers who can answer questions, an opportunity to meet other patients, and even distractions such as music and videos could help to decrease this source of stress.

Education

More and more nurses are becoming involved in clinical trials in both research and community hospitals. Nursing educators need to provide content on the development of new cancer therapies and the phases of human trials involved. They may then address the practical and ethical issues involved in these trials. Case studies based on these findings may be presented for discussion in the classroom,

giving nursing students more insight into their patients' experience. An understanding of the impact of clinical trials on patients may also enable instructors and students to explore specific interventions such as those suggested above.

Research

The preliminary findings of this study need to be expanded and explored in other settings and with other patient populations. For example, researchers might examine the characteristics of other participants in Phase I trials and compare them with these 20 participants. Are those patients who come to Phase I trials a unique population? Are they more sophisticated and proactive than the average cancer patient? Or were these participants different from most, and if so, why were they? Also, it might be important to question whether participants in Phase II and randomized Phase III trials also display similar characteristics.

There are many other remaining questions. Is the Internet taking the place of the family physician or augmenting this traditional resource? How can we as clinicians best serve these particular consumers of health care? If patients are seeking clinical trials and investigators are seeking participants, how can they be brought together in the most efficient way? Finally, how can patients be protected and supported when they decide to

seek investigational treatment? What is the actual relationship between risks and benefits in these early trials? It may be different from what has traditionally been assumed. Further qualitative studies with Phase I clinical trials may uncover more of the participants' understanding of these risks and benefits.

Policy Making

These participants on Phase I trials demonstrated more autonomy and less vulnerability to coercion than previously suggested, answering some ethical concerns about informed consent. However, there remains the justice issue of equal access for all patients with advanced cancer who have no standard therapy available to them. If those patients who come to participate in Phase I clinical trials are primarily those who have the resources to find the trials on their own, then all cancer patients may not have equal access to these trials. Researchers and policy makers need to look for ways to overcome barriers faced by those who lack such resources as health insurance, access to the Internet, and the means to travel.

Transportation, for example, has been found to be a major barrier to treatment for poor and minority patients (Guidry et al., 1997). Since 1990, the National Cancer Institute has been specifically concerned with the problem of low accrual of ethnic minority patients to clinical trials (Roberson, 1994). In order to recruit these

patients to Phase I and later trials, it may be necessary to provide or subsidize transportation. In addition, while information on clinical trials is readily available on the Internet, it may not be accessible to those of lower socio-economic status. Perhaps more use of radio and television spots would increase awareness among these more vulnerable patients. Understanding some of the experience of these participants may suggest other ways in which ethical and policy decisions need to be made.

In summary, the findings of this study, while not generalizable, can provide valuable insights into the way cancer patients experience Phase I clinical trials. Clinicians can extrapolate from these findings to their own patients to better understand and support them, educators can teach students about this experience to prepare them for their care of patients on trials, researchers can plan studies to confirm and extend the findings, and policy makers can use the data in strategies to increase accrual of vulnerable patients to clinical trials.

Patient.....
Examiner.....
Date.....

"MINI-MENTAL STATE"

Maximum Score	Score		
		ORIENTATION	
5	( )	**What is the (year) (season) (date) (day) (month)?**	
5	( )	**Where are we: (state) (county) (town) (hospital) (floor)**	
		REGISTRATION	
3	( )	**Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he learns all 3. Count trials and record.**	**Trials**
		ATTENTION AND CALCULATION	
5	( )	**Serial 7's. 1 point for each correct. Stop after 5 answers. Alternatively spell "world" backwards.**	
		RECALL	
3	( )	**Ask for the 3 objects repeated above. Give 1 point for each correct.**	
		LANGUAGE	
9	( )	**Name a pencil, and watch (2 points)** **Repeat the following "No ifs, ands or buts." (1 point)** **Follow a 3-stage command:** **"Take a paper in your right hand, fold it in half, and put in on the floor" (3 points)** **Read and obey the following:** **CLOSE YOUR EYES (1 point)** **Write a sentence (1 point)** **Copy design (1 point)**	

_____ **Total score**

ASSESS level of consciousness along a continuum _____
Alert Drowsy Stupor Coma

INSTRUCTIONS FOR ADMINISTRATION OF
MINI-MENTAL STATE EXAMINATION

ORIENTATION

(1) Ask for the date. Then ask specifically for parts omitted, e.g., "Can you also tell me what season it is?" One point for each correct.
(2) Ask in turn "Can you tell me the name of this hospital?" (town, county, etc.). One point for each correct.

REGISTRATION

Ask the patient if you may test his memory. Then say the names of 3 unrelated objects, clearly and slowly, about one second for each. After you have said all 3, ask him to repeat them. This first repetition determines his score (0-3) but keep saying them until he can repeat all 3, up to 6 trials. If he does not eventually learn all 3, recall cannot be meaningfully tested.

ATTENTION AND CALCULATION

Ask the patient to begin with 100 and count backwards by 7. Stop after 5 subtractions (93, 86, 79, 72, 65). Score the total number of correct answers.
If the patient cannot or will not perform this task, ask him to spell the word "world" backwards. The score is the number of letters in correct order. E.g. dlrow = 5, dlorw = 3.

RECALL

Ask the patient if he can recall the 3 words you previously asked him to remember. Score 0-3.

LANGUAGE

Naming: Show the patient a wrist watch and ask him what it is. Repeat for pencil. Score 0-2.

Repetition: Ask the patient to repeat the sentence after you. Allow only one trial. Score 0 or 1.

3-Stage command: Give the patient a piece of plain blank paper and repeat the command. Score 1 point for each part correctly executed.

Reading: On a blank piece of paper print the sentence "Close your eyes", in letters large enough for the patient

to see clearly. Ask him to read it and do what it says. Score 1 point only if he actually closes his eyes.

Writing: Give the patient a blank piece of paper and ask him to write a sentence for yo. Do not dictate a sentence, it is to be written spontaneously. It must contain a subject and verb and be sensible. Correct grammar and punctuation are not necessary.

Copying: On a clean piece of paper, draw intersecting pentagons, each side about 1 in., and ask him to copy it exactly as it is. All 10 angles must be present and 2 must intersect to score 1 point. Tremor and rotations are ignored.

Estimate the patient's level of sensorium along a continuum, from alert on the left to coma on the right. (Folstein et al., 1975, pp. 196-198)

Appendix B

Interview Schedule

Introduction

I am interested in your experience of participating in a clinical trial (or study). Anything you can tell me about that experience will be valuable to me.

Of course, you need not answer any question if you do not care to, and you many end this interview at any time. If you become tired, please tell me right away so that we may end the interview.

Sample Questions and Prompts

To begin with, please describe the study (trial) in which you are participating.

Possible prompts:
- What is the study about?
- What is involved in the study?
- Who can take part in the study?

How did you come to participate in this study (trial)?

Possible prompts:
- How did you find out about the study?

Some people have difficulty deciding to participate in a clinical trial, and others decide fairly easily. What kind of decision process did you go through in thinking about whether or not to participate?

Possible prompts:
- What particular things were you concerned about?
- What influenced you to take part in this study?
- Who helped you to decide to take part?

What did you expect when you enrolled in this trial (study)?

Possible prompts:
- What did you think would happen?
- What were you told about the study?

How has your participation in this study (trial) been different from what you expected?

Possible prompts:
- Which of the things you were expecting came true?

Which of the things you were expecting did not come true?

How do you think your participation in this study (trial) has affected you?

Possible prompts:
What about you has changed during the time that you've been on the study?
How has your health changed during the time that you've been on the study?
How has your quality of life changed during the time that you've been on the study?

How do you feel about the study (trial) now that you have been participating in it?

Possible prompts:
What you do like about being part of this study?
What do you not like about being part of this study?

Suppose you were asked by another cancer patient whether or not he or she should take part in a clinical trial like this. What would you tell him or her?

Is there anything that you would like to add?

Appendix C

Demographic Data

Age: _____

Gender: M [ ] F [ ]

Ethnicity: _____

Primary cancer diagnosis: _____

Time since diagnosis: _____

Employment status:

Full-time	[ ]
Part-time	[ ]
Unemployed	[ ]
Retired	[ ]
Disabled	[ ]

Marital status: Sgl [ ] Mar [ ] Wid [ ] Sep [ ] Div [ ]

Religion: _____

Level of education:

Less than high school	[ ]
High school graduate	[ ]
Some college	[ ]
College graduate	[ ]

Household income:

<$15,000	[ ]
$15,000 - 30,000	[ ]
$30,001 - 45,000	[ ]
$45,001 - 60,000	[ ]
>$60,000	[ ]

Appendix D

Informed Consent Forms

OS-95-8

INFORMED CONSENT

TITLE: The Experience of Cancer Patients Participating in Phase I Clinical Trials

DEPARTMENT: Nursing

PRINCIPAL INVESTIGATOR: Carol H. Mack, RN, MN, PhD(c), OCN

24 HOUR PHONE (EMERGENCY): [redacted])

PURPOSE: The purpose of this research study is to describe what the experience of taking part in a clinical trial is like.

PROCEDURE: If you decided to take part in this study you will be asked to describe your actual experience of participating in a clinical trial. First, a simple test of thinking and memory will be given to you. This test involves answering a few questions and following directions and takes no more than ten minutes. The purpose of this test is to make sure that your cancer or your cancer treatment has not interfered with your ability to concentrate in an interview. Next, you will be asked to answer questions about your experience in an interview with a nurse researcher who works with cancer patients. The interview will be tape recorded. This interview may take as long as an hour to an hours and a half, but you may end it at any time. Several weeks later, you will be interviewed again to see if anything has changed about your experience. You may be interviewed two or three times over several months.

RISKS: The risks and discomforts of this study are possible upset or embarrassment from sharing feelings and possible fatigue from taking part in a long interview. If at any time, you wish to talk with a therapist about feelings which have come up in the interview, one will be available to you.

BENEFITS: Some people who participate in interviews benefit from having the change to tell their story. In addition, the information gathered may benefit future patients by giving doctors and nurses a better understanding of what it is like

for patients who are in clinical trials.

ALTERNATIVES: The alternative is to not participate in this study.

CONFIDENTIALITY: The confidentiality of your medical records for this study will be maintained by the investigators and the Research Committee (IRB). Specific study-related information will be made available to the sponsor and the National Cancer Institute. The Food and Drug Administration (FDA) will be allowed access to your medical records. Unless required by law, the FDA will maintain the confidentiality of your medical records.

OFFER TO ANSWER QUESTIONS: Your treatment will be under the care of Dr. _____ at phone _____ who you may contact with any questions or concerns regarding your treatment. Any questions or concerns that you may have about treatment related injuries should be discussed with the Principal Investigator, Carol Mack, RN, MN, OCN at [redacted]

COERCION AND WITHDRAWAL STATEMENT: Your decision whether or not to participate will not interfere with your future care at this institution. If you decided to participate, you are free to withdraw your consent and to discontinue participation at any time.

INJURY STATEMENT: If you require medical treatment as a result of injury arising from your participation in this study, the financial responsibility for such will be yours.

FINANCIAL RESPONSIBILITY STATEMENT: There is no financial cost to you for participating in this study.

NEW INFORMATION: Any new information that is developed during the course of research which may relate to your willingness to continue or discontinue participation in this study will be provided to you.

HUMAN RIGHTS IN MEDICAL STUDIES: California State Law requires that you must be informed about:

1. The nature and purpose of the study.
2. The procedures in the study and any drug or device to be

used.
3. Discomforts and risks to be expected from the study.
4. Benefits to be expected from the study.
5. Alternative procedures, drugs or devices that might be helpful and their risks and benefits.
6. Availability of medical treatment should complications occur.
7. The opportunity to ask any questions about the study or the procedure.
8. The opportunity to withdraw at any time without affecting your future care at this institution.
9. A copy of the written consent form for the study.
10. The opportunity to consent freely to the study without the use of coercion.
11. Statement regarding liability for physical injury, if applicable.

If you have any questions or concerns regarding these rights or the character of the study, please feel free to discuss them with the person(s) conducting the study or you may contact the Research Committee Chairman at the LAC-USC Medical Center, Trailer 25. Tel. Number [redacted].

AGREEMENT: Your signature indicates that you have decided to participate having read the information provided above as well as the human right in medical studies and that you understand your rights for participation in this study. You will receive a copy of the signed Informed Consent.

Please print or type Patient Name	Please print or type Witness Name	Date
Signature of Patient	Signature of Witness	Date
Signature of Investigator		Date

CONSENT TO PARTICIPATE IN RESEARCH

The Experience of Cancer Patients Participating in Phase I Clinical Trials

You are invited to participate in a research study conducted by Carol H. Mack, RN, MN, OCN, from the School of Nursing at the University of California, Los Angeles. The results of this study will contribute to her dissertation. You were selected as a possible participant in this study because you have agreed to take part in a Phase I clinical trial.

- **PURPOSE OF THE STUDY**

The purpose of this research study is to describe what the experience of taking part in a clinical trial is like.

- **PROCEDURES INVOLVED IN PARTICIPATING IN THE STUDY**

If you volunteer to participate in this study, we would ask you to do the following things:

First, you will take a simple test of thinking and memory. This test involves answering a few questions and following directions and takes no more than ten minutes. The purpose of this test is to make sure that your cancer or your cancer treatment has not interfered with your ability to concentrate in an interview.

Next, you will answer questions about your experience in an interview with a nurse researcher who works with cancer patients. This interview may take place in a clinic room or in your home or any other place in which you feel comfortable. The interview will be tape recorded. It may take as long as an hour to an hour and a half, but you may end it at any time.

Several weeks later, you will be interviewed again to see if anything has changed about your experience. You may be interviewed a maximum of three times over six months.

- **POTENTIAL RISKS AND DISCOMFORTS**

The risks and discomforts of this study are possible upset or embarrassment from sharing feelings and possible fatigue from taking part in a long interview. If at any time, you wish to

talk with a counselor about feelings which have come up in the interview, one will be available to you.

- **POTENTIAL BENEFITS TO SUBJECTS**

Some people who participate in interviews benefit from having the chance to tell their story.

- **POTENTIAL BENEFITS TO SOCIETY**

The information gathered in this study may benefit future patients by giving doctors and nurses a better understanding of what it is like for patients who are in clinical trials.

- **PAYMENT FOR PARTICIPATION**

There is no payment for your participation in this study.

- **CONFIDENTIALITY**

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your written permission or as required by law. Confidentiality will be maintained by means of recording your name separately from your interview transcript. Also, if this study is published, your name and information about you will be removed or disguised.

- **PARTICIPATION AND WITHDRAWAL**

Your participation is VOLUNTARY. Your decision whether or not to participate will not affect your relationship with UCLA or your doctor. If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without penalty. The investigator may withdraw you from this research if circumstances arise which warrant doing so. If this should happen, you will be told the reason for your withdrawal.

- **IDENTIFICATION OF INVESTIGATORS**

If you have any questions or concerns about your participation in the research, please feel free to contact either of the following:

Principal Investigator: Carol H. Mack, RN, MN, OCN [redacted]

Faculty Advisor: Nancy Anderson, RN, C, PhD
School of Nursing
University of California, Los Angles
[redacted]

- **RIGHTS OF RESEARCH SUBJECTS**

You may withdraw your consent at any time and discontinue participation without penalty. You are not waiving any legal claims, rights or remedies because of your participation in this research study. If you have questions regarding your rights as a research subject, contact the Office for Protection of Research Subjects, UCLA, Box 951694, Los [redacted]

SIGNATURE OF RESEARCH SUBJECT

My signature indicates that I have read and understand the information provided above, and that I willingly agree to participate in this research study. **I WILL RECEIVE A COPY OF THIS FORM.**

Signature of Research Subject _____ Date _____

SIGNATURE OF WITNESS

Signature of Witness (optional, or if present) _____ Date _____

SIGNATURE OF INVESTIGATOR OR APPROVED DESIGNEE

Signature of Investigator or Approved Designee _____ Date _____

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