

Integrating Palliative Care for Patients on Clinical Trials: Opportunities for Oncology Nurses

Betty Ferrell¹, Tami Borneman¹, Anna Cathy Williams¹, Angela Scardina², Patricia Fischer², Thomas J. Smith²

¹Division of Nursing Research and Education, City of Hope National Medical Center, Duarte, CA, ²Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA



Corresponding author: Betty Ferrell, RN, PhD, MA, FAAN, FPCN, CHPN

Division of Nursing Research and Education, City of Hope National Medical Center, Medical Center

Tel: 626-218-2825; Fax: 626-301-8941

E-mail: bferrell@coh.org

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ABSTRACT

The purpose of this article is to describe the lessons learned in the course of a 5-year research study on a palliative care intervention for persons on a Phase 1 clinical trial. Patients who are participating in Phase 1 trials and the families who care for them may be especially vulnerable and require special attention. The patients are generally experiencing the effects of advanced disease, and they also may soon experience unknown side effects, intense treatment regimens, and the emotional stress of an uncertain future as a result of clinical trial participation. Oncology nurses in all roles including clinical trials/research nurses, clinicians, educators, and advanced practice registered

nurses play a critical role in addressing the quality-of-life concerns in this population. Palliative care can provide better symptom control and information on treatment options and facilitate a better understanding of patient/family goals. Attending to these factors can ultimately mean improved survival for the advanced cancer patient, and support for these patients can assist in advancing the field of oncology as these investigational therapies hold the promise for enhancing survival.

Key words: Clinical trials, oncology nursing, palliative care, Phase 1 trials, quality of life

Introduction

Cancer patients participating in clinical trials represent a vulnerable population in need of expert nursing care.^[1-5] These patients are generally experiencing advanced disease

and have received traditional treatments and now are considered for investigational therapies as a last treatment option. While patients on such trials may represent a group

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with higher functional status, they also may soon experience unknown side effects, intense treatment regimens, and the emotional stress of an uncertain future.^[6,7]

The authors of this paper have recently concluded a 5-year (2015–2019) randomized trial testing a palliative care intervention for patients with solid tumors entering Phase I trials.^[8] The following discussion presents the lessons learned from this trial and a summary of key recommendations for oncology nurses. The paper also summarizes key literature which has described the clinical trial population and their need for support.

Oncology nurses in all roles including clinical trials/research nurses, clinicians, educators, and advanced practice registered nurses (APRNs) play a critical role in addressing the quality-of-life (QOL) concerns in this population. Support for these patients can assist in advancing the field of oncology as these investigational therapies hold the promise for enhancing survival.

Background

Patients who are participating in Phase 1 trials and the families who care for them may be especially vulnerable and require special attention.^[2-4,9] Palliative care can be particularly helpful for patients and families by enabling better communication about the goals of care with physicians and within families.^[10] Palliative care can provide better symptom control and information on treatment options and facilitate a better understanding of patient/family goals.^[11-15] Attending to these factors can ultimately mean improved survival for the advanced cancer patient.

Phase 1 patients are generally the most “well” of advanced cancer patients. Despite this, they often have a significant symptom burden, with greater symptom severity than other oncology patients. Phase 1 trials may increase a patient’s existing symptom burden as the trial drugs may have substantial toxicities and result in new side effects.^[16,17] These additional factors may result in an increased number of clinic visits for the patient, substantial time away from family, and added caregiver distress. Emotional distress can also be a predominant factor in this group as they face the uncertainty of unknown outcomes from trials. Phase 1 patients also often do not have advance care directives and have not designated a proxy decision maker. The focus on continuing treatment through trials may delay access to palliative care.

In addition, studies have shown that Phase 1 patients may fail to understand the treatment intent of the trial, and their expectations about the benefits and risks of the Phase 1 trial may be unrealistic. These patients and their families may not understand the right to withdraw from the trial or not to enter it at all. Patients may not fully comprehend their prognosis, the severity of their illness,

and the fact that in many cases their illness is terminal, with or without Phase 1 trial participation. Even when physicians inform patients of the very small chance they will respond to a Phase 1 treatment, patients often remain hopeful about having a treatment response. In one report, 90% of Phase 1 patients would risk an unproven drug with a 10% chance of mortality.^[18] In this same report, 84% were aware of hospice and palliative care options, but only 6% had considered it for themselves. More recent data – albeit not from Phase I patients – suggest that at least in some health systems, people have a much more realistic view of their circumstances, with only 7% persisting to say they could be cured when that was not medically possible.^[15]

Studies have shown that a patient’s decision to enroll in a Phase 1 trial is a difficult time because this marks a transition in the disease trajectory and a critical decision point. Phase 1 trials are intended for first testing of agents in humans, dose determination, and toxicity monitoring, yet patients often believe that they may offer a cure.^[1-3] New targeted agents and immunotherapies may prolong survival, but most patients will not realize the disease benefit or extended life. The completion of a Phase 1 trial often means the end of cancer treatment with high mortality in the months that follow.^[6,7,19]

Lessons learned

The following is a summary of five key lessons derived from the literature and the research of the authors for oncology nurses. The lessons are also summarized in Appendix 1.

Lesson 1: Advances in cancer treatments have changed the patient experience

For example, up to 20% of advanced lung cancer patients are living 5 years after starting immunotherapy, unheard of with chemotherapy.^[20]

Lesson 2: Participation in clinical trials amidst advanced disease evokes psychosocial and spiritual distress

Appendix 2 presents a summary of the care plan information from patients in the authors’ recently completed study of integrating palliative care for patients on Phase 1 trials.^[5,8] Patients in one of the two study sites are routinely asked to identify “sources of hope, worry, and joy.” Prominent themes were hope for “more time,” for positive response to the cancer treatment, and for improved QOL. The responses indicate that patients were hopeful that the Phase 1 trial would prolong life or improve QOL. There was a strong agreement that joy came from family and relationships. These comments illustrate the myriad of emotions faced by patients on trials. Oncology nurses can support these patients’ other supportive care services. Chaplaincy is also a valuable end-of-life care need.

Lesson 3: Palliative care should be implemented early in the course of disease and treatment

There is a very strong body of evidence supporting the benefits of early referral to palliative care.^[3,7,16,21,22] Studies have documented the impact of palliative care on improved physical symptoms, psychological symptoms, distress, QOL, family caregiver QOL outcomes, and spiritual well-being.^[21-27] The research also supports enhanced benefit when palliative care is implemented early in the course of the disease and treatment rather than in the last weeks to months of life. Educating the patient on supportive and palliative care options during treatment helps with both symptom management and the patient's sense of hope. This education, post diagnosis and then regularly thereafter, would be beneficial to the patient, as well as to the local providers. Making providers aware of community palliative care resources would enable better patient support and be beneficial to treatment plans.

This lesson is of special importance in the clinical trial population where research has also documented that these patients may avoid palliative care consultation even when recommended by their oncology clinicians as they fear this may distract from their disease-focused care on a clinical trial and continued hope for prolonged survival or cure.^[28-32]

Oncology nurses are central to efforts to integrate palliative care and support patients and their families in understanding that this care will enhance their participation in the trial and that evidence also supports that survival is increased by receiving palliative care. Research and clinical teams need to have discussions about prognosis to work more cohesively together.

Lesson 4: Symptoms are a common experience related to clinical trials requiring aggressive assessment and treatment

There is well-established understanding in oncology nursing that symptom management is fundamental to quality patient care. Patients participating in clinical trials are often the most important group for symptom management as they experience the combined effects of symptoms related to advancing disease, side effects of previous treatments, and now the potential for both known and unknown effects of investigational treatments.^[33-35]

There is increased emphasis in oncology on the need for aggressive symptom management beginning with comprehensive, patient-reported symptom assessment.^[32-35] Patients also are often fearful of developing new symptoms from investigational therapies, and the ability to control symptoms can greatly impact trial eligibility, accrual, and retention.^[36]

There are numerous assessment tools available to assess symptoms and to support quality improvement efforts to insure optimum symptom management.^[37-39] The authors'

research with Phase 1 trial patients has included the use of the PRO-CTCAE tool, a patient-reported measure of common toxicities and symptoms.^[32] Appendix 3 presents a summary of the symptoms we have found to be frequent in the clinical trial population and essential to assess routinely. These symptoms also have a significant impact on QOL.

Our experience which is strongly supported in the literature is that without the use of a structured symptom assessment, patients are unlikely to report all of the symptoms they are experiencing. An additional challenge in this population is that patients may choose to not report their symptoms for fear that they will not qualify for a trial or will not be able to continue on a trial or treatment.

Oncology nurses can be strong advocates to advance symptom assessment and management and also to develop patient and family teaching for symptom management. Early referral to palliative care services is also helpful to add their expertise in managing complex symptoms as well as to anticipate and treat symptoms from trials and those problems associated with advancing disease and the end of life. The work of the research and clinical teams and all disciplines needs to be coordinated in order to provide more cohesive patient management, which, in turn, will yield better patient outcomes.

Lesson 5: The transition beyond clinical trial participation is an understudied and critical time in the cancer trajectory

A very important lesson the authors have identified from their research in this population is the need for attention to the transition beyond clinical trial participation. Our research related to palliative care for patients on Phase 1 trials was prompted by recognition that often when a trial ends, the patient may feel lost in transition. Many patients are reluctant to leave care in the clinical trial setting if referred from the community, and the community oncologist and staff may feel unprepared to resume care. Some patients in our study understood this trial to be the last treatment option, whereas others assumed that there would be additional trials to enroll in or major advances in care during their time of trial participation.

Our research and extensive literature also documents that patients completing trials have very high mortality; in our study of 479 patients, the median survival was 10 months. These patients had low referral rates to palliative care and to hospice, and for those referred to hospice, there was late referral. In addition, these patients had low rates of advance directive completion.

There is a great opportunity for oncology nurses to improve the care provided following clinical trial participation to insure transition in care. Clinicians who will continue to provide care for these patients will also need information regarding the potential side effects or delayed

effects of the trial. Structured handoffs have improved care in nearly every situation tried, and should be applied to Phase I handoffs back to oncology or palliative care.^[40]

This time of transition beyond clinical trial participation is not only one of the treatment changes, but also a time of enhanced significant psychological and social needs. Patients and families benefit greatly during this time from interdisciplinary care to support these needs.

Summary

The care of oncology patients in the future will include the increasing emphasis on investigational therapies. Building strong support systems will benefit not only the individual patients and families on these trials, but also all future patients as cancer care is enhanced through advances in care. Oncology nursing is essential in every aspect of this care.

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Conflicts of interest

There are no conflicts of interest.

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Appendixes

Appendix 1: Lessons learned

Lesson 1: Advances in cancer treatments have changed the patient experience.

Lesson 2: Participation in clinical trials amidst advanced disease evokes psychosocial and spiritual distress.

Lesson 3: Palliative care should be implemented early in the course of disease and treatment.

Lesson 4: Symptoms are a common experience related to clinical trials requiring aggressive assessment and treatment.

Lesson 5: The transition beyond clinical trial participation is an understudied and critical time in the cancer trajectory.

Appendix 2: Sources of hope, worry, and joy

“What are you hoping for?”

More time:

- With spouse, children, grandchildren
- To get back to work
- To live a normal life – Get married, raise children, watch them grow up

That dying will not take long

Quality of life:

- Maintain quality of life
- Highest quality of life for as long as possible.

Hopes that treatment will:

- Control the disease
- Alleviate the pain
- Cure/eliminate the disease
- Prevent further decline
- Extend life
- Manage the symptoms for the rest of life
- If this doesn't work, that there will be another trial

“What makes you worry the most?”

Fear of worsening disease or death:

- How I may die – be a vegetable and linger
- That disease is getting worse
- Uncertain future
- Dying

- New trial will not work because last one did not
- Waiting between treatments

Quality-of-life issues:

- Sexual ability
- Anxiety
- Depression
- Loss of control
- Effects of next round of chemo
- Fear of needing further emergency surgery

Family:

- Wife and family
- This was supposed to be the time to retire, travel, be with wife
- Being there for 7-year-old son
- Daughter will not have a strong family network nearby
- Son battling drug addiction
- Wants children to know she will do whatever it takes to beat this cancer
- That her son will have to be her primary caregiver
- Will not have supportive care when she needs it

“What brings you joy?”

- Family
- Grandchildren
- Social life, events
- Work
- Hobbies.

Appendix 3: Common symptoms in patients in clinical trials

- Attention/memory/concentration
- Cardiovascular
 - Palpitations
 - Arm or leg swelling
 - Tremors.
- Cutaneous
 - Hair loss
 - Skin problems
 - Problems with nails
 - Hand and foot syndrome
 - Acne
 - Skin burns from radiation
- Gynecology/urinary
 - Frequent urination
 - Urinary urgency
- Gastrointestinal
 - Decreased appetite
 - Constipation
 - Bloating
 - Diarrhea
 - Heartburn
 - Nausea/vomiting
 - Taste problems
 - Hiccups
- Mood
 - Anxiety
 - Depression
- Neurological
 - Numbness in hands and feet
 - Dizziness
- Oral
 - Dry mouth
 - Difficulty swallowing
 - Mouth sores/skin cracking
- Pain
 - Headache
- Respiration
 - Dyspnea
 - Cough
- Sexuality
 - Sexual interest
 - Sexual function
- Sleep
 - Insomnia
 - Fatigue
- Visual
 - Blurred vision
- Other
 - Hot flashes
 - Ringing in ears
 - Bruising
 - Sweating.