JOURNAL OF PALLIATIVE MEDICINE
Volume 17, Number 12, 2014

DOI: 10.1089/jpm.2014.0108

Feasibility of a Palliative Care Intervention for Cancer Patients in Phase I Clinical Trials

Virginia Sun, RN, PhD,[1] Liz Cooke, RN, MN, ANP, AOCN, PMHNP-BC,[2] Vincent Chung, MD, FACP,[3] Gwen Uman, PhD,[4] Thomas J. Smith, MD, FACP,[5] and Betty Ferrell, PhD, FAAN, FPCN[1]

Abstract

Background: Cancer patients with advanced disease who have exhausted most treatment options are often offered participation in Phase I clinical trials. To date, studies that assess the benefits of palliative care provided concurrently in Phase I clinical trial settings are lacking. The overall purpose of this study was to test the feasibility of a palliative care intervention administered concurrently to cancer patients receiving treatment in a Phase I clinical trial.

Methods: Cancer patients enrolling in a Phase I clinical trial were invited to participate in this study. Patients completed baseline questionnaires prior to treatment initiation that assessed quality of life (QOL), symptom distress, psychological distress, and satisfaction with care. Patients then received the palliative care intervention (PCI), which consisted of comprehensive QOL assessment, care planning for the patient during an interdisciplinary team meeting, and two patient education sessions. Patients were surveyed again at 1 and 2 months following treatment initiation.

Results: A total of 14 patients were accrued to the pilot over a 3-month time period, representing 70% of eligible patients. Patient retention was high at 1 month (75%), and had declined at 2 months (50%). Patient outcome measure scores, including symptom distress, psychological distress, and satisfaction with care, were relatively stable over time, except for overall QOL, which declined over time.

Conclusions: Concurrent palliative care is feasible for cancer patients treated in Phase I clinical trial settings. A large, multisite randomized controlled trial based on this pilot will be launched to test the efficacy of the intervention in this understudied cancer population.

Introduction

Despite significant progress in research and treatments, many cancer patients will be diagnosed with or progress to advanced disease. Participation in a Phase I clinical trial, in most situations, is one of the few possibly curative treatment options left for patients with advanced cancer.[1] Enrollment in a clinical trial can be demanding for patients and families, with the extra burden of frequent outpatient visits for tests and treatments. Phase I patients are generally among the most functionally well of cancer patients, to meet study criteria, but they experience symptom burdens similar to those of other cancer patients.[2] After adjustments for performance status scores, Phase I patients were more likely to report an average of five or more symptoms, and had higher symptom severity for an average of six symptoms.[3]

Phase I patients are a highly motivated group willing to take chances on treatment. In one report, 90% of Phase I patients would risk an unproven drug with a 10% chance of mortality.[4] In this same report, 84% were aware of hospice and palliative care options, but only 6% had considered these for themselves. Patients who elect to participate in cancer clinical trials and their physicians often feel that patients must forgo or delay palliative care. Participation in clinical trials precludes enrollment in hospice in most settings. Patients and families participating in clinical trials, including Phase I trials, can be especially vulnerable, and therefore they may need

[1]Division of Nursing Research and Education, Department of Population Sciences, [2]Department of Hematology and Hematopoietic Transplantation, [3]Department of Medical Oncology and Therapeutics Research, City of Hope, Duarte, California.
[4]Vital Research, Inc., Los Angeles, California.
[5]Sidney Kimmel Comprehensive Cancer Center of the Johns Hopkins Medical Institutions, Baltimore, Maryland.
Accepted May 12, 2014.

special attention. Patients enrolled in Phase I clinical trials could potentially benefit from palliative care concurrently, yet limited evidence is available to support such a change in care. In this brief report, we describe the feasibility of a concurrent, interdisciplinary palliative care intervention (PCI) for patients in Phase I clinical trials.

Methods

The design of the PCI was based on a current National Cancer Institute (NCI)-funded Program Project Grant (BF, principal investigator), in which interdisciplinary care coordination and patient education served as key components of the intervention.[5–8] Advanced practice nurses (APNs) who were not involved in the usual care of clinical trial patients completed a comprehensive assessment of the patient's quality of life (QOL) needs using baseline questionnaires. Using findings from the comprehensive assessment, patient cases were presented during an interdisciplinary care meeting attended by treating oncologists, nurses, and supportive care services including palliative medicine, social work, chaplaincy, rehabilitation, and nutrition. Care coordination and recommendations were made by the interdisciplinary care team that were tailored to each patient's needs, and referrals to supportive care services were initiated as needed. Patients then received two educational sessions, with content organized in four QOL domains: physical, psychological, social, and spiritual well-being (see Table 1). Patients received written materials that contained information on all topics in both sessions. At the beginning of each session patients were presented with a list of common physical, social, psychological, and spiritual concerns, and they were then asked to identify three topics for discussion during each session. This provided for tailoring of the content to the patient's needs and preferences. Family members were allowed to participate in the educational sessions, but this was not a requirement.

Patients were recruited from the medical oncology ambulatory clinics of an NCI-designated comprehensive cancer center in Southern California. Study procedures and protocol were approved by the center's Institutional Review Board. Inclusion criteria included the following: 1) patients diagnosed with solid tumors who were assessed and who signed an informed consent for participation in a Phase I clinical trial; and 2) age 21 or older.

An APN approached all eligible patients during a regularly scheduled clinic visit. Following informed consent, patients completed baseline assessment. Comprehensive assessment of QOL needs for each patient was undertaken, and assessment results were presented to the interdisciplinary care team during weekly care meetings. The APN then administered the two patient education sessions prior to patients receiving the first dose of Phase I investigational treatment. Supportive care referrals were made based on interdisciplinary care team recommendations. Patients were reevaluated at 1 and 2 months following study enrollment.

Outcome measures included the following: 1) Functional Assessment of Cancer Therapy-General (FACT-G) for QOL[9]; 2) Functional Assessment of Chronic Illness Therapy-Spirituality (FACIT-Sp-12) for spiritual well-being[10]; 3) Memorial Symptom Assessment Scale (MSAS) for symptom intensity and distress, used to assess symptom distress[9,11]; 4) Distress Thermometer for psychological distress[12]; and 5) FAMCARE-Patient scale for patient satisfaction with care.[13,14] Data were entered into a relational database and

Table 1. Patient Education Session Content

Session	*Content*
#1	Focus on physical and social well-being Tailor content Discuss physical/symptoms and social concerns Provide recommended resources Coordinate for needed follow-up
#2	Focus on psychological and spiritual well-being Questions from previous session Tailor content Discuss psychological and spiritual concerns Provide recommended resources Coordinate for needed follow-up Summarize contents covered

Table 2. Sociodemographic and Clinical Characteristics (N = 14)

	N	%
Gender		
Male	9	64.3
Female	5	35.7
Age		
Mean (range)	52.4 (38–68)	
Race/Ethnicity		
Caucasian	6	42.9
Hispanic/Latino	4	28.6
African American	2	14.3
Asian	1	7.1
Other	1	7.1
Highest level of education		
High school	7	50.0
College	5	35.7
Graduate/Professional school	2	14.3
Marital status		
Married	8	57.1
Never arried	3	21.4
Divorced	2	14.3
Widowed	1	7.1
Type of cancer		
Breast	3	21.4
Colorectal	3	21.4
Renal cell carcinoma	2	14.3
Hepatobiliary	2	14.3
Ovarian	1	7.1
Head and neck	1	7.1
Lung	1	7.1
Prostate	1	7.1
Years since diagnosis		
Mean	5 (1–21)	
Comorbidities[a] ($n = 11$)		
None	2	18.2
Cardiovascular	8	72.8
Depression	3	27.3
Diabetes	2	18.2
Central nervous system	1	9.1
Gastrointestinal	1	9.1

[a]Subjects can select more than one answer.

audited for accuracy. Descriptive statistics were computed, and distributions were examined for normality. Nonparametric analysis was used, as is appropriate for sample sizes of 20 or fewer subjects. The Friedman nonparametric test of summed ranks was used to test for within subjects change over time (baseline, 1 month, and 2 months).

Results

A total of 14 patients were accrued over a 3-month time period, representing 70% of eligible patients. Retention was 78.5% at 1 month and 50% at 2 months, and this was primarily due to physical decline or death. Ten patients were able to receive the first dose of Phase I experimental therapeutics while also concurrently being enrolled in the PCI pilot study. Mean age was 52 years, and the majority of patients were male. More than half of the patients were ethnic minorities (57.1%) and were married. The most common cancer diagnoses in this cohort included breast (21.4%), colorectal (21.4%), kidney (14.3%), and hepatobiliary cancers (14.3%). The median time since diagnosis was 5 years. Detailed demographic characteristics are provided in Table 2.

Table 3. Differences Pre- and Postintervention for Key Variables

	Mean (SD)	*Median*	*Interaction* p *value*
Psychological distress (Distress Thermometer)			
Range = 0–10; 0 = no distress, 10 = extreme distress			
Baseline	3.0 (2.1)	2.0	
Month 1	2.6 (2.2)	3.0	0.083
Month 2	5.0 (2.7)	5.0	
Global Distress Index (GDI of the MSAS)			
Range = 0–4; higher score = more symptom distress			
Baseline	1.6 (1.3)	1.1	
Month 1	1.4 (0.8)	1.7	0.964
Month 2	1.7 (0.9)	2.2	
Total symptom score (MSAS)			
Range 1–4; higher score = higher symptom burden			
Baseline	1.2 (0.9)	0.6	
Month 1	1.2 (0.7)	1.0	0.867
Month 2	1.3 (0.6)	1.2	
Total QOL score (FACT-G)			
Range = 0–108			
Baseline	72.1 (7.1)	73.0	
Month 1	62.2 (9.1)	62.0	0.050
Month 2	64.1 (12.9)	62.5	
Spiritual well-being (FACIT-Sp-12)			
Range = 0–48			
Baseline	28.9 (6.0)	28.0	
Month 1	23.6 (5.9)	24.3	0.062
Month 2	29.0 (7.0)	28.0	
Satisfaction with care (FAMCARE-Patient)			
Range 1–5; higher score = more satisfaction with care			
Baseline	4.5 (0.4)	4.4	
Month 1	4.1 (0.3)	4.1	0.204
Month 2	4.3 (0.4)	4.3	

FACIT-Sp-12, Functional Assessment of Chronic Illness Therapy-Spirituality; FACT-G, Functional Assessment of Cancer Therapy-General; MSAS, Memorial Symptom Assessment Scale; QOL, quality of life; SD, standard deviation.

On average, it took the APN about 10 minutes to present each patient case during the interdisciplinary care meetings. The APN was able to complete the two patient education sessions within 1 to 1.5 months following enrollment. Each patient education session lasted approximately 45 minutes, and the majority of the teaching was completed in two sessions.

Overall, there were no statistically significant differences for patient outcomes across the three time points, except for the total FACT-G score ($p = 0.05$), where scores for months 1 and 2 were lower than baseline (see Table 3). Although scores for all other outcomes, including psychological distress, total symptom score, and spiritual well-being, changed across the three time points, these differences were not statistically significant.

Discussion

In this feasibility study, we determined that early integration of interdisciplinary palliative care, as coordinated by an APN, is feasible for patients treated concurrently in Phase I clinical trials. This study has now led to an NIH-funded, multisite randomized study that will test the efficacy of early, concurrent palliative care for patients in Phase I clinical trials.

Although we were successful in accruing and sustaining patients in the study, several feasibility challenges were encountered during this pilot study experience (see Table 4). The close collaboration with medical oncologists and clinical trial nurse coordinators was helpful in identifying the ideal time for enrolling patients into the pilot study. As Phase I clinical trial patients typically undergo an extended period of eligibility screening prior to treatment, we were able to administer the intervention prior to treatment initiation. This extended period of Phase I clinical trial eligibility screening may be the ideal time to intervene for this population, when patients may benefit more from initiation of supportive care services and anticipation of expected symptoms before treatment begins. Attrition was anticipated to be a challenge in this population of patients with advanced cancer, and many patients were too ill to continue with study participation. Nevertheless, we were able to retain at least half of the patients in this small cohort through the 2-month study period. Close collaboration and communication with clinical trial nurse coordinators is essential for understanding patient's status during treatment, and

Table 4. Feasibility Challenges Encountered in Pilot Study

Challenges	*Potential solutions*
Timing of accrual	• Close collaboration with Phase I clinical trial group, medical oncology, and clinical trial nurse coordinators.
Attrition/ Retention	• Close collaboration and communication with clinical trial nurse coordinators to follow patient status in Phase I clinical trials. • Patients who discontinue participation on Phase I clinical trials will be retained and supported in palliative care study.
Patient education sessions	• Content can be administered in one instead of two sessions when necessary to meet the patient's needs. • Education session can be administered either in-person or via telephone.

can aid in anticipating potential attrition. Patients who discontinue participation in Phase I clinical trials would be able to continue with the PCI. Finally, flexibility with the mode of delivery of the patient education session, such as allowing for content to be delivered in one versus two sessions if requested by the patient, could help ensure that patients receive all components of the intervention.

We observed declines in patient outcomes over the 2-month study period, but these changes were not statistically significant. Observations of QOL declines in terminally ill cancer patients have been reported, and it has been proposed that the pre-terminal phase in cancer patients is characterized by multiple parameters of decline in QOL, a period that has been termed the ''longitudinal terminal decline QOL model.''[15] The declines seen in our study were relatively small, suggesting that key outcomes such as symptom distress, psychological distress, and QOL were somewhat stable over 2 months for the patients. This in turn suggests that concurrent palliative care, as administered through our intervention, may have potential in preventing the precipitous declines in QOL reported in other studies. Indeed, in a study that described time course and characteristics of QOL in terminally ill patients, Kutner and colleagues found that pain, nonpain physical and psychological symptoms, and QOL were all relatively stable.[16] Most of the patients in this study were enrolled in hospice care and were already benefiting from palliative care. Stabilization of QOL for cancer patients who are terminally ill may be as equally important as statistically significant improvements in overall QOL prior to death.

In conclusion, very few PCIs are designed and tested for cancer patients receiving treatment in Phase I clinical trials. Cancer patients are expected to experience steeper declines in QOL compared with noncancer patients, and Phase I clinical trial patients fit this criterion.[17] These patients may benefit from interdisciplinary palliative care that supports hope for symptom relief, psychosocial support, and better understanding of their treatment options and goals while they are concurrently receiving disease-directed therapies.

Acknowledgments

We thank Carin Van Zyl, MD, Marianna Koczywas, MD, Arti Hurria, MD, and Cy Stein, MD, PhD, for support of study accrual and implementation.

Author Disclosure Statement

No competing financial interests exist.

References

1. Fu S, Barber FD, Naing A, Wheler J, Hong D, Falchook G, Piha-Paul S, Tsimberidou A, Howard A, Kurzrock R: Advance care planning in patients with cancer referred to a phase I clinical trials program: The MD Anderson Cancer Center experience. J Clin Oncol 2012;30:2891–2896.
2. Hui D, Parsons H, Nguyen L, Palla SL, Yennurajalingam S, Kurzrock R, Bruera E: Timing of palliative care referral and symptom burden in phase 1 cancer patients. Cancer 2010;116:4402–4409.
3. Finlay E, Lu HL, Henderson H, O'Dwyer PJ, Casarett DJ: Do phase 1 patients have greater needs for palliative care compared with other cancer patients? Cancer 2009;115:446–453.
4. Agrawal M, Grady C, Fairclough DL, Meropol NJ, Maynard K, Emanuel EJ: Patients' decision-making process regarding participation in phase I oncology research. J Clin Oncol 2006;24:4479–4484.
5. Ferrell B, Koczywas M, Grannis F, Harrington A: Palliative care in lung cancer. Surg Clin North Am 2011;91:403–417, ix.
6. Grant M, Sun V, Fujinami R, Sidhu R, Otis-Green S, Juarez G, Klein L, Ferrell B: Family caregiver burden, skills preparedness, and quality of life in non-small cell lung cancer. Oncol Nurs Forum 2013;40:337–346.
7. Koczywas M, Cristea M, Thomas J, McCarty C, Borneman T, Del Ferraro C, Sun V, Uman G, Ferrell B: Interdisciplinary palliative care intervention in metastatic non-small-cell lung cancer. Clin Lung Cancer 2013;14:736–744.
8. Koczywas M, Williams AC, Cristea M, Reckamp K, Grannis FW Jr, Tiep BL, Uman G, Ferrell B: Longitudinal changes in function, symptom burden, and quality of life in patients with early-stage lung cancer. Ann Surg Oncol 2013;20:1788–1797.
9. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, Silberman M, Yellen SB, Winicour P, Brannon J: The functional assessment of cancer therapy scale: Development and validation of the general measure. J Clin Oncol 1993;11:570–579.
10. Peterman AH, Fitchett G, Brady MJ, Hernandez L, Cella D: Measuring spiritual well-being in people with cancer: The functional assessment of chronic illness therapy—Spiritual Well-being Scale (FACIT-sp). Ann Behav Med 2002;24:49–58.
11. Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Kiyasu E, Sobel K, Coyle N, Kemeny N, Norton L, et al.: The memorial symptom assessment scale: An instrument for the evaluation of symptom prevalence, characteristics and distress. Eur J Cancer 1994;30A:1326–1336.
12. National Comprehensive Cancer Network. Clinical practice guidelines in oncology. Distress Management. 2013. www.nccn.org (last accessed April 8, 2014).
13. Lo C, Burman D, Rodin G, Zimmermann C: Measuring patient satisfaction in oncology palliative care: Psychometric properties of the FAMCARE-Patient scale. Qual Life Res 2009;18:747–752.
14. Lo C, Burman D, Hales S, Swami N, Rodin G, Zimmermann C: The FAMCARE-Patient scale: Measuring satisfaction with care of outpatients with advanced cancer. Eur J Cancer 2009;45:3182–3188.
15. Hwang SS, Chang VT, Fairclough DL, Cogswell J, Kasimis B: Longitudinal quality of life in advanced cancer patients: Pilot study results from a VA medical cancer center. J Pain Symptom Manage 2003;25:225–235.
16. Kutner JS, Bryant LL, Beaty BL, Fairclough DL: Time course and characteristics of symptom distress and quality of life at the end of life. J Pain Symptom Manage 2007;34:227–236.
17. Downey L, Engelberg RA: Quality-of-life trajectories at the end of life: Assessments over time by patients with and without cancer. J Amr Geriatr Soc 2010;58:472–479.

Address correspondence to:
Virginia Sun, RN, PhD
Division of Nursing Research and Education
Department of Population Sciences
City of Hope
1500 East Duarte Road
Duarte, CA 91010

E-mail: vsun@coh.org