

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

ALLIANCE A221303

RANDOMIZED STUDY OF EARLY PALLIATIVE CARE INTEGRATED WITH STANDARD ONCOLOGY CARE VERSUS STANDARD ONCOLOGY CARE ALONE IN PATIENTS WITH INCURABLE LUNG OR NON-COLORECTAL GASTROINTESTINAL MALIGNANCIES

A Limited Access Study

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Study Resources:

Medidata Rave® iMedidata portal
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Questions related to data submission, RAVE or patient follow-up:	Data Manager
Questions regarding the protocol document and model informed consent:	Protocol Coordinator
Questions related to IRB review:	Alliance Regulatory Inbox [REDACTED]
Questions regarding CTEP-AERS reporting:	Regulatory Affairs Manager [REDACTED]

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VERSUS STANDARD ONCOLOGY CARE ALONE IN PATIENTS WITH INCURABLE LUNG AND NON-COLORECTAL GASTROINTESTINAL MALIGNANCIES**

Study Patient Participant Eligibility Criteria (see Section 3.2)

- Confirmed incurable lung cancer (NSCLC, small cell lung cancer, or mesothelioma) or non-colorectal GI cancer (esophageal, gastric, hepatic, biliary, pancreatic or GI unknown primary) not being treated with curative intent
- Informed of diagnosis of incurable disease within the previous 8 weeks.
- Age \geq 18 years
- ECOG Performance Status 0-2
- Ability to read and respond to questions in English or able to complete questions with minimal assistance required from an interpreter or family member.
- Planning to receive medical care for cancer at the enrolling institution
- Participants must be under the care of an oncologists (who does not practice as a palliative care physician for that patient), but their current plan may or may not include chemotherapy or other forms of tumor-directed therapies.

**Required Initial
Laboratory Values**

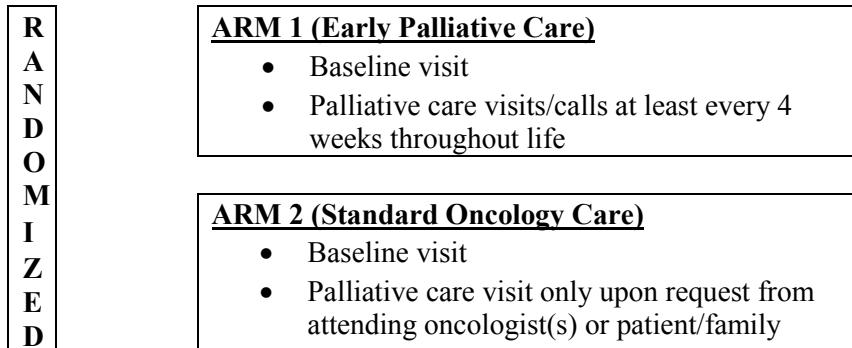
None

Study Family Caregiver Participant Eligibility Criteria (see Section 3.3)

- Relative or friend who is identified by the patient participant who plans to regularly accompany the patient to the majority of their clinic visits.
- Family caregiver must live with the patient or have in-person contact with him or her at least twice per week.
- Ability to read and respond to questions in English or able to complete questions with minimal assistance required from an interpreter or family member.
- Age \geq 18 years

Note: An eligible patient may participate in this trial without an eligible family caregiver being registered.

Schema



Patients: Complete questionnaires at baseline, 6, 12 and 24 weeks

Family caregivers: Complete questionnaires at baseline, 6, 12 and 24 weeks

Please refer to the full protocol text for a complete description of the eligibility criteria and intervention plan.

The outpatient palliative care (PC) clinic must be either (1) located within the Cancer Center or (2) the palliative care clinicians have the ability to see patients at the Cancer Center, and the palliative care clinic (or PC team) must be led by a board certified PC physician. At least the lead PC staff at each participating institution (ideally, as many as possible at each institution) must complete two 1-hour web-based training courses.

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1.0 BACKGROUND

1.1 Introduction

Despite improvements in cancer therapy, the prognosis of incurable lung and non-colorectal gastrointestinal cancers remains poor with median survivals of less than one year.¹ During the course of illness, these patients often experience marked physical suffering, psychological distress and resource-intensive care at the end-of-life (EOL).^{2,3} While cancer treatment may extend survival, the improvement on quality-of-life (QOL) and distress is minimal for these patients.⁴ Moreover, anti-cancer therapy delivered at the EOL may negatively impact quality of death, family caregiver bereavement, the cost of health care delivery in the U.S., and survival.^{3,5,6} Studies to date demonstrate a compelling need for interventions that not only diminish suffering but also improve the quality and delivery of care for patients who have both a short-life expectancy and high symptom burden.⁷

Palliative care focuses on providing expert symptom management and psychosocial support for patients and families with serious illnesses.⁸ However, traditionally palliative care clinicians do not provide longitudinal care in the outpatient setting and are often consulted to see patients only near the EOL.^{9,10} We completed a randomized study of early, integrated palliative and oncology care versus standard oncology care alone in patients with newly diagnosed metastatic non-small cell lung cancer to assess whether early involvement of palliative care is beneficial.¹¹ The palliative care model in this trial entailed board-certified palliative care physicians and advanced practice nurses who conducted their clinic visits in the Cancer Center and on the same day as the patients' oncology visit. Patients were scheduled for visits with the palliative care team at a minimum of every three weeks, although more frequent visits were permitted. If patients were admitted to the hospital, they were also followed by the hospital-based inpatient palliative care team throughout their admission. We observed significant improvements in patient reported outcomes (QOL, mood and illness understanding) and several key measures of quality EOL care and resource utilization (chemotherapy near death, documentation of EOL care preferences, and length of stay in hospice).¹¹⁻¹⁴ Despite less chemotherapy at the EOL and greater hospice utilization, patients assigned to early palliative care (PC) had prolonged survival of over two months, compared with patients receiving standard care. While these results are exciting, this study was a single institution study and it is unclear if these findings will be reproduced in a multi-site trial.

Recently, the American Society of Clinical Oncology (ASCO) published a Provisional Clinical Opinion that early palliative should be considered for any patients with metastatic cancer.¹⁵ Therefore, an urgent need exists to evaluate the early, integrated palliative care model in a larger number of cancer populations and across multiple care settings. No palliative care studies have been conducted through the cooperative group mechanism to date.

A multi-site cooperative group study will be the most effective way to determine if the early palliative care model can be disseminated and if the findings are reproducible. We have assembled a team with significant experience in conducting early palliative care trials (Temel, Jackson, Greer) and in completing supportive care interventions in the cooperative group (Loprinzi).

1.2 Rationale and Significance

Symptom burden in patients with incurable lung and gastrointestinal cancer and their families: Patients with incurable solid tumors experience high rates of both physical and psychological distress.^{16,17} Symptoms such as pain, fatigue, dyspnea, and nausea lead to a poor QOL and are associated with high rates of depression and anxiety.¹⁸ The family members of these patients also frequently experience emotional, physical and financial distress when caring for loved ones with incurable cancers.^{19,20} Despite advances in cancer care, life expectancy remains limited for

patients with incurable malignancies, such as lung and non-colorectal gastrointestinal (GI) cancer, which account for more than half of cancer-related deaths in men and one-third in women.²¹⁻²⁴ These patients have a median survival of less than one year and often receive limited benefit from chemotherapy, usually with progression of disease after only a few months of treatment.²⁵ While chemotherapy may improve symptoms, the impact on QOL is less clear as patients also experience marked side effects and toxicities from anti-cancer therapies, causing physical and emotional suffering.⁴ Impairments in QOL and mood not only compromise the wellbeing of patients with incurable cancer and their families, but also predict lower rates of survival.²⁶⁻²⁸ Typically, patients with incurable lung and non-colorectal GI cancers experience a high symptom burden, which begins at the time of diagnosis, persists throughout the course of disease, and intensifies near the end-of-life.²⁹ Interventions should occur early in the course of incurable disease and demonstrate a meaningful impact on the suffering of patients with poor prognosis cancers and their family caregivers.

Aggressive cancer care at the end-of-life: Oncology care for patients with incurable cancer is becoming increasingly aggressive with greater use of multiple anti-cancer regimens and administration of chemotherapy near the EOL.³⁰ Over the last decade, rates of admission to the hospital, emergency department, and intensive care unit during the final month of life have increased as well.^{31,32} Unfortunately, aggressive medical treatment at the EOL fails to improve survival in patients with incurable cancer and correlates negatively with family caregivers' perceptions of the quality of EOL care.^{3,33,34} Such care also places family caregivers at increased risk of major depression and complicated bereavement.³ Since U.S. hospice agencies generally lack the financial resources to provide anti-cancer therapy, administration of chemotherapy and inpatient stays at the EOL often interrupt or delay referrals to hospice services.^{3,35,36} Late referral to hospice prevents patients from accessing comprehensive EOL services that benefit the entire family.³⁷ Specifically, family members of patients who receive hospice services not only report greater satisfaction with care and higher quality of death for the patient, but also experience improved psychological and physical health outcomes, compared with those caring for patients who do not receive hospice.³⁸ Thus, the American Society of Clinical Oncology Quality Oncology Practice Initiative (ASCO QOPI) has recognized several key metrics for determining high quality EOL care including: no chemotherapy in the last 14 days of life, referral to hospice and length of stay in hospice > 3 days.³⁹

End-of-life decision-making in advanced cancer: The majority of patients with advanced cancer and their families report a desire to receive timely and realistic prognostic information.⁴⁰⁻⁴⁵ Data demonstrate that patients with incurable cancer and their families often fail to understand the goals of therapy and maintain inaccurate illness perceptions. A recent study revealed that only half of patients with a new lung cancer diagnosis accurately recalled information about the goal of treatment 1-3 days after their oncology visit.⁴⁶ However, a recent study demonstrated that patients who received early palliative care retained or developed an accurate assessment of their prognosis compared to those patients receiving standard oncology care (82% compared to 59%, respectively).⁴⁷ Importantly, patients' understanding of their illness and prognosis strongly predicts treatment decision-making at the EOL.⁴⁸⁻⁵⁰ While patients with advanced cancer who view themselves as terminally ill are more likely to prefer and receive symptom directed care, those who overestimate their prognosis are more likely to choose an aggressive course of therapy.^{33,51}

Impact of early palliative care on symptom burden, quality-of-life and end-of-life care: The benefits of palliative care in the inpatient setting are well established in the literature.^{9,52} However, examining the impact of palliative care in the outpatient care setting represents a relatively newer focus of research.⁵³ Several previous investigations have evaluated the utility of intermittent or telephone-based palliative care interventions in the outpatient care setting, demonstrating positive effects on some salient patient-reported outcomes.^{54,55} We have studied

a more clinically based integrated service model in which palliative and oncology care provide simultaneous care throughout the course of illness. After completing a pilot feasibility study of this integrated care model, we performed a randomized controlled trial in patients with incurable lung cancer, observing significant improvements in QOL and quality of care at the end-of-life.^{11,53} We are currently performing a similar study in a broader population of patients with advanced thoracic and gastrointestinal cancers. In addition to assessing many patient-reported and health care utilization measures, we are collecting abundant qualitative and quantitative data on the nature of the palliative care service in the outpatient care setting. This information will allow us to study the early palliative care model in a multi-site trial.

1.3 Hypotheses

Aim 1: To determine the efficacy of early, integrated palliative care (PC) on patient and family caregiver reported outcomes in those with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer.

- Hypotheses 1: Compared to patients receiving standard care (SC), patients receiving early PC will (1) experience improved QOL and fewer depressive symptoms; and (2) report a more accurate understanding of their terminal illness and the goals of care.
- Hypotheses 2: Compared to family caregivers in the SC arm, family caregivers of patients receiving early PC will (1) experience improved QOL and fewer depressive symptoms throughout the course of the patient's illness; and (2) report a more accurate understanding of the patient's terminal illness and the goals of care.

Aim 2: To assess the impact of early, integrated PC on quality of EOL care and resource utilization in patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer

- Hypotheses: Compared to patients receiving SC, patients receiving early PC will (1) receive higher quality EOL care (i.e., less chemotherapy in the last 14 days of life, greater utilization of hospice services, and/or length of stay in hospice > 3 days); (2) experience less hospital and ICU days and (3) have at least the same survival as patients receiving standard care

1.4 Study Design

This study will be a randomized, controlled trial of early PC integrated with standard oncology care versus standard oncology care alone. Patients will be randomized in a 1:1 fashion between study arms. The dynamic allocation procedure was adopted to balance the marginal distributions of stratification: tumor type (lung vs. esophageal/gastric vs. hepatic/biliary/pancreatic/ unknown primary), and family caregiver participation (yes vs. no).⁵⁶ We modeled this study design to be identical to the completed and ongoing trial at the Massachusetts General Hospital (MGH) Cancer Center. We are not randomizing by site (i.e. cluster-randomized design) due to several reasons: (1) Although such a design would reduce contamination effects, it introduces site effects that could also impact outcomes; (2) In both of our prior trials, there was minimal contamination with few patients in the standard care arm referred for PC in the outpatient care setting; and (3) Within Alliance, ensuring equivalent sites across geographical regions with the same PC resources would be challenging. We have also decided not to include an attention control group as the logistical and sample size requirements for a third study arm would be substantial. Additionally, the observed clinical benefits of PC in our previous investigation did not appear to be merely due to increased clinician time with patients and families but related to the expertise of PC clinicians. We anticipate including approximately 20 Alliance sites with a minimum of 10 community sites with an enrollment goal of at least 15 patients per site.

1.5 Description of Intervention

The study intervention consists of the early integration of palliative care services into standard oncology care in an outpatient setting for patients with advanced lung and non-colorectal gastrointestinal malignancies who are not being treated with curative intent. The palliative care services provided to patients randomized to the intervention will be provided by board-certified physicians and/or advanced practice nurses and will focus on the following areas: (1) developing and maintaining the therapeutic relationship with the patients and family caregivers; (2) assessing and treating patient symptoms; (3) providing support and reinforcement of coping with advanced cancer in patients and family caregivers; (4) assessing and enhancing prognostic awareness and illness understanding in patients and family caregivers; (5) assisting with treatment decision-making; and (6) end-of-life care planning.

Palliative care services in the community are likely to be highly variable and there are no standard practices for outpatient palliative care at this time. Thus, to promote the use of more uniform palliative care practices for patients at the differing study sites, the PC service from each participating institution will be required to meet specific eligibility requirements and at a minimum, the lead PC member will be required to complete two web-based training courses on providing palliative care services to patients.

We have included minimum requirements for participating palliative care services in Section 12.1 under 'Institutional credentialing' to be as inclusive as possible. Also, to ensure reproducible and measurable intervention, study sites will be provided with guidelines for the palliative care visits in the form of a manual, which is based on our previous studies. The data used to generate this manual, revealed six key elements of PC visits (relationship and rapport building, addressing symptoms, addressing coping, establishing illness understanding, discussing cancer treatments, end-of-life planning and engagement family members).⁵⁷

2.0 OBJECTIVES

2.1 Primary objectives

To determine the efficacy of early integrated palliative care (PC) on patient reported QOL at 12 weeks using the FACT in patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer.

2.2 Secondary objectives

- 2.2.1 To determine the efficacy of early integrated palliative care (PC) on other patient reported outcomes in patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer, by assessing the endpoints detailed in Section 11.4.1.1.
- 2.2.2 To determine the efficacy of early integrated palliative care (PC) on family caregiver reported outcomes in those with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer, by assessing the endpoints detailed in Section 11.4.1.2.
- 2.2.3 To assess the impact of early, integrated PC on quality of EOL care and resource utilization in patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer by assessing the endpoints detailed in Section 11.4.1.3.
- 2.2.4 To determine concordance between patient and family caregiver report of prognosis/curability.

3.0 PATIENT SELECTION

For questions regarding eligibility criteria, see the Contact Information page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.1 On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this intervention is appropriate.

Although they will not be considered formal eligibility (exclusion) criteria, physicians should recognize that the following may seriously increase the risk to the patient entering this protocol:

- Psychiatric illness which would prevent the patient from giving informed consent.

3.2 Study Patient Participant Eligibility Requirements

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate.

— **3.2.1 Documentation of Disease:**

— Confirmed incurable lung cancer (NSCLC, small cell lung cancer, or mesothelioma) or non-colorectal GI cancer (esophageal, gastric, hepatic, biliary, pancreatic or GI unknown primary) not being treated with curative intent.

— **3.2.2 Informed of diagnosis of incurable disease within the previous 8 weeks.**

— **3.2.3 Age \geq 18 years**

— **3.2.4 ECOG Performance Status 0-2**

— **3.2.5 Ability to read and respond to questions in English** or able to complete questions with minimal assistance required from an interpreter or family member.

— **3.2.6 Planning to receive all medical care for cancer at the enrolling institution.**

— **3.2.7 Participants must be under the care of an oncologist (who does not practice as a palliative care physician for that patient),** but their current plan may or may not include chemotherapy or other forms of tumor-directed therapies.

3.3 Study Family Caregiver Participant Eligibility Requirements

Use the spaces provided to confirm one family caregiver's eligibility by indicating Yes or No as appropriate.

— **3.3.1 Relative or friend who is identified by the patient participant who plans to regularly accompany the patient to the majority of their clinic visits.**

— **3.3.2 Family caregiver must live with the patient or have in-person contact with him or her at least twice per week.**

— **3.3.3 Ability to read and respond to questions in English or able to complete questions with minimal assistance required from an interpreter or family member.**

— **3.3.4 Age \geq 18 years**

Note: An eligible patient may participate in this trial without an eligible family caregiver being registered.

4.0 PATIENT REGISTRATION

4.1 CTEP Investigator Registration Procedures

Food and Drug Administration (FDA) regulations and National Cancer Institute (NCI) policy require all investigators participating in any NCI-sponsored clinical trial to register and to renew their registration annually.

Registration requires the submission of:

- a completed Statement of Investigator Form (FDA Form 1572) with an original signature
- a current Curriculum Vitae (CV)
- a completed and signed Supplemental Investigator Data Form (IDF)
- a completed Financial Disclosure Form (FDF) with an original signature

Fillable PDF forms and additional information can be found on the CTEP website at <http://ctep.cancer.gov/investigatorResources/investigator_registration.htm>. For questions, please contact the CTEP Investigator Registration Help Desk by email at

[REDACTED].

4.2 CTEP Associate Registration Procedures / CTEP-IAM Account

The Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) application is a web-based application intended for use by both Investigators (i.e., all physicians involved in the conduct of NCI-sponsored clinical trials) and Associates (i.e., all staff involved in the conduct of NCI-sponsored clinical trials).

Associates will use the CTEP-IAM application to register (both initial registration and annual re-registration) with CTEP and to obtain a user account.

Investigators will use the CTEP-IAM application to obtain a user account only. (See CTEP Investigator Registration Procedures above for information on registering with CTEP as an Investigator, which must be completed before a CTEP-IAM account can be requested.)

An active CTEP-IAM user account will be needed to access all CTEP and CTSU (Cancer Trials Support Unit) websites and applications, including the CTSU members' website.

Additional information can be found on the CTEP website at <http://ctep.cancer.gov/branches/pmb/associate_registration.htm>. For questions, please contact the **CTEP Associate Registration Help Desk** by email at

[REDACTED].

4.3 CTSU Site Registration Procedures

This study is supported by the NCI Cancer Trials Support Unit (CTSU).

IRB Approval:

Each investigator or group of investigators at a clinical site must obtain IRB approval for this protocol and submit IRB approval and supporting documentation to the CTSU Regulatory Office before they can be approved to enroll patients. Study centers can check the status of their registration packets by querying the Regulatory Support System (RSS) site registration status page of the CTSU members' website by entering credentials at <https://www.ctsu.org>. For sites under the CIRB initiative, IRB data will automatically load to RSS.

4.3.1 Submitting Regulatory Requirements

Submit required forms and documents to the CTSU Regulatory Office, where they will be entered and tracked in the CTSU RSS.

CTSU Regulatory Office



4.3.2 Checking Your Site's Registration Status

Check the status of your site's registration packets by querying the RSS site registration status page of the members' section of the CTSU website. (Note: Sites will not receive formal notification of regulatory approval from the CTSU Regulatory Office.)

- Go to <https://www.ctsu.org> and log in to the members' area using your CTEP-IAM username and password
- Click on the Regulatory tab at the top of your screen
- Click on the Site Registration tab
- Enter your 5-character CTEP Institution Code and click on Go

4.4 Registration Requirements

4.4.1 Informed consent:

The patient must be aware of the neoplastic nature of his/her disease and willingly consent after being informed of the intervention, the experimental nature of the intervention, alternatives, potential benefits, and discomforts. Current human protection committee approval of this protocol and a consent form is required prior to patient consent and registration. Patients may be enrolled in other clinical trials while participating in this study.

4.4.2 Limited Access and Site Credentialing

This is a limited access study. Each participating Alliance member site must be individually approved by the study chair or designate and be listed as a participating site on the cover page of the protocol. All participating sites will be approved by the study chair prior to being listed on the protocol cover page. See also Sections 5.3 and 12.0.

The confirmation of site participation eligibility by the study chair is required before any patients may be enrolled on this study.

4.4.3 Patient/Family Caregiver Completed Booklets

Patient and family caregiver assessment questionnaire booklets for A221303 are to be ordered prior to the registration of any patients.

Questionnaire booklets are to be ordered prior to the registration of any patients and family caregivers. Booklets can be ordered by downloading and completing the QOL booklet order form (located under the 'Supplemental Documents' section of the A221303 study web page on the Alliance member website) and faxing the form to the Mayo Operational Support Clerk at [REDACTED]. Samples of the booklets are found in Appendices II and III, which are to be used for reference and IRB submission only. They are not to be used for patient or family caregiver completion.

4.5 Patient Registration/Randomization

Patient enrollment will be facilitated using the Oncology Patient Enrollment Network (OPEN). OPEN is a web-based registration system available on a 24/7 basis. To access OPEN, the site user must have an active CTEP-IAM account (check at < <https://eapps-ctep.nci.nih.gov/iam/index.jsp> >) and a 'Registrar' role on either the LPO or participating organization roster.

All site staff will use OPEN to enroll patients to this study. It is integrated with the CTSU Enterprise System for regulatory and roster data and, upon enrollment, initializes the patient in the Rave database. OPEN can be accessed at <https://open.ctsu.org> or from the OPEN tab on the CTSU members' side of the website at <https://www.ctsu.org>. A user manual is available for OPEN users on the CTSU site.

Prior to accessing OPEN, site staff should verify the following:

- All eligibility criteria have been met within the protocol stated timeframes.
- All patients have signed an appropriate consent form and HIPAA authorization form (if applicable).

Note: The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

Further instructional information is provided on the OPEN tab of the CTSU members' side of the CTSU website at <https://www.ctsu.org> or at <https://open.ctsu.org>. For any additional questions contact the CTSU Help Desk at [REDACTED].

4.5.1 Family Caregiver Participation

Family caregiver consent and eligibility is captured on the OPEN enrollment form. Participating family caregivers must have signed and dated all applicable consents and authorization forms and source documents should be kept with the patient record.

See section 4.5 regarding OPEN site staff verification and OPEN access requirements.

Note: An eligible patient may be enrolled in this study with or without the enrollment of an eligible family caregiver.

4.6 Stratification Factors

4.6.1 Tumor type: lung vs. esophageal/gastric vs. hepatic/biliary/pancreatic/unknown primary

4.6.2 Family caregiver participation: yes vs. no.

4.7 Study Arm Assignments

4.7.1 The factors defined in Section 4.4 will be used as stratification factors.

4.7.2 After the patient has been registered into the study, the values of the stratification factors will be recorded, and the patient will be assigned to one of the following study groups using the Pocock and Simon dynamic allocation procedure⁵⁵ which balances the marginal distributions of the stratification factors between the two groups.

- Early palliative care
- Standard oncology care

5.0 STUDY IMPLEMENTATION

5.1 Palliative Care Clinic Requirements

Institutions must have an outpatient palliative care clinic that meets the study site requirements listed in Section 12.1 for participation in this trial. Participating institutions need to be approved for participation by the study chair, or the study chair's designate.

5.2 Palliative Care Physician and Advanced Practice Nurse Requirements

The outpatient clinic leadership must include a physician and/or advanced practice nurses board certified in palliative care. See Section 12.2.

5.3 Palliative Care Manual and Training Requirements

5.3.1 General Requirements

Palliative care clinicians participating in this study are required to follow the guidance and instructions for the palliative care intervention as detailed in the 'Early Integration of Palliative and Oncology Care: An Intervention Manual' as Appendix I of this protocol. Please refer to this manual for guidance regarding the implementation of the palliative care intervention, as well as, the training requirements for administering palliative care for the PC team at each study site. These guidelines should be reviewed prior to initiating this trial.

Palliative care clinicians will be required to:

1. Review the 'Early Integration of Palliative and Oncology Care: An Intervention Manual' in its entirety; and
2. At least one leader of the outpatient palliative care clinic must complete registration with CTEP (see Sections 4.1 and 4.2), *if not currently registered*;
3. At least one leader of the outpatient palliative care clinic must complete the two web-based training courses, each approximately 1-hour in length:
 - Site Staff: Palliative Care Training Video One
 - Site Staff: Palliative Care Training Video Two
4. At least one leader of the outpatient palliative care clinic must be willing to participate in phone conference calls with the protocol leadership every 1-2 month to discuss any issues that arise during this protocol.

5.3.2 PC Web-based Training

The goal of the training courses will be to educate the clinicians on ways in which the provision of outpatient palliative care differs from inpatient delivery models. These courses will be informed by the educational needs assessment and focus on two areas: (1) Psychosocial aspects of outpatient palliative care, specifically the cultivation of prognostic awareness and the promotion of adaptive patient coping strategies over the course of the illness; and (2) developing a collaborative practice with oncology clinicians through role definition and joint patient visits.

The Web-based training module can be found at <https://www.phscpd.org/palliativecarewebinars>. Full instructions for completing the web-based training are located in Appendix VI)

If you have any issues or questions please contact the Partners Office of Continuing Professional Development at [REDACTED].

5.4 Patient Recruitment

Oncology clinicians will offer study participation to eligible patients. Some suggested language to help the oncology clinician discuss the protocol with eligible patients is included in Appendix V. Willing participants will provide written informed consent and receive a signed copy of the consent form. Also, family caregivers (e.g., relative or friend) upon whom the patient relies for help and who will likely accompany them to clinic visit will be asked to enroll. We will invite this person to participate in the family caregiver portion of the study.

- Family caregivers will be eligible to enroll and provide written informed consent on the same day as the patient. Patients and family caregivers who provide consent will complete the baseline participant reported measures.
- Patients without a willing family caregiver will not be excluded from study participation. Patients and family caregivers who provide written informed consent will complete study measures, including a demographic questionnaire.
- Patients who decline study entry, but desire early palliative care referral based on their preference, may be referred to palliative care based on the individual Cancer Center's standard protocol or approach.

6.0 DATA SUBMISSION

6.1 Data collection and submission

Data collection for this study will be done exclusively through the Medidata Rave clinical data management system. Access to the trial in Rave is granted through the iMedidata application to all persons with the appropriate roles assigned in Regulatory Support System (RSS). To access Rave via iMedidata, the site user must have an active CTEP-IAM account (check at <<https://eapps-ctep.nci.nih.gov/iam/index.jsp>>) and the appropriate Rave role (Rave CRA, Read-Only, Site Investigator) on either the LPO or participating organization roster at the enrolling site.

Upon initial site registration approval for the study in RSS, all persons with Rave roles assigned on the appropriate roster will be sent a study invitation e-mail from iMedidata. To accept the invitation, site users must log into the Select Login (<https://login.imedidata.com/selectlogin>) using their CTEP-IAM user name and password, and click on the “accept” link in the upper right-corner of the iMedidata page. Please note, site users will not be able to access the study in Rave until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learnings (eLearnings), and can be accessed by clicking on the link in the upper right pane of the iMedidata screen.

Users that have not previously activated their iMedidata/Rave account at the time of initial site registration approval for the study in RSS will also receive a separate invitation from iMedidata to activate their account. Account activation instructions are located on the CTSU website, Rave tab under the Rave resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on iMedidata/Rave is available on the CTSU members' website under the Rave tab at www.ctsu.org/RAVE/ or by contacting the CTSU Help Desk at [REDACTED]. The accompanying tables in the following subsections detail the schedule of administration of assessment tools for patients (Section 6.2) and family caregivers (Section 6.3). Questionnaires will be completed as described below for each group.

At each scheduled assessment time, the site staff will document participant compliance (patient and family caregiver) with study questionnaires, noting whether the participants completed questionnaires on time as well as the method of administration (e.g., via in-person or phone

interview). For those participants who fail to complete questionnaires, the site staff will note the reason for noncompliance.

Patient and family caregiver assessment questionnaire booklets for A221303 are to be ordered prior to the registration of any patients. Samples of questionnaire/booklets are available in Appendices II and III, respectively, for reference and IRB submission only. They are not to be used for patient or family caregiver completion. Booklets must be given to patients and family caregiver to complete, and they should be instructed to return the booklets to site staff either in person or by mail. Site staff will enter patient and family caregiver responses into the Medidata Rave database.

6.2 Patient Reported Measures

Site staff will administer the questionnaires for patient reported measures during the time scheduled as detailed in the table below and are included as Appendix III. They will review each questionnaire with the patient and instruct the patient to complete as much of the questionnaire as possible. It is anticipated that the patient reported measures will take approximately 15-20 minutes to complete based on previous experience administering similar questionnaires in this patient population. Patient and family caregiver assessment questionnaires are not required once patients are in hospice care.

Data submission schedule for questionnaires to be completed by the patient:

Form	Baseline	6* Weeks	12* Weeks	24* Weeks
Demographics	X			
<u>As applicable</u>				
For lung – FACT-L; OR For esophageal and gastric – FACT-E; OR For hepatic, biliary and pancreatic – FACT-Hep	X	X	X	X
HADS	X	X	X	X
PTPQ		X	X	X

*+- 2 weeks before or after each time point for completion of the self-report measures will be allowed.

6.3 Family Caregiver Reported Measures

Site staff will administer the questionnaires for family caregiver reported measures during the time scheduled as detailed in the table below which are included as Appendix IV. They will review each questionnaire with the family caregiver and instruct the family caregiver to complete as much of the questionnaire as possible. It is anticipated that the family caregiver measures will take approximately 10 minutes to complete based on previous experience administering similar questionnaires to the family caregiver population.

Data submission schedule for questionnaires to be completed by the family caregiver:

Form	Baseline	6* Weeks	12* Weeks	24* Weeks
Demographics	X			
SF-36	X	X	X	X
HADS	X	X	X	X
PTPQ		X	X	X

*+- 2 weeks before or after each time point for completion of the self-report measures will be allowed.

6.4 Chart Abstraction

The following data regarding measures of health service utilization and EOL care will be submitted using Medidata Rave® through chart abstraction by site staff at 1, 2, and 3 years (from enrollment) and at death.

6.4.1 Administration of anticancer therapy

- Chemotherapy: For each line of therapy, note name of agent, route of administration (intravenous or oral) and dates of administration.
- Radiation therapy: For each course of radiation therapy course, note site treated and dates of administration.

6.4.2 Enrollment to hospice: (yes [date of enrollment]/no)

6.4.3 Hospital Care

- Emergency room visits: For each emergency room visit, note reason for visit and date and if patient was hospitalized (yes/no)
- Hospital admissions: For each hospital admission, note reason for admission, dates of admission, and documented code status.
- ICU admissions: For each ICU admission, note reason for ICU admission and dates of admission

6.4.4 Date and location of death

6.4.5 The number of PC visits (in both the outpatient and inpatient setting) for participants in each study group and the reason for PC referral for patients assigned to standard care

6.4.6 Referrals to other supportive care services, including social work, chaplain and psychiatry/psychology and referring provider

7.0 INTERVENTION

During registration, patients will be randomized to receive either early palliative care (Arm 1) or standard oncology care (Arm 2).

Over the course of the study patients and their family caregivers in both arms will be asked to complete questionnaires about quality-of-life, mood, and their perception of prognosis and treatment goals during regularly scheduled oncology clinical visits at baseline and week 6, 12, and 24 visits.

7.1 Early Palliative Care Arm

The intervention will be comprised of one baseline visit and palliative care visits or phone calls (if a clinic visit is not feasible) at least every four weeks throughout the patient's life.

7.1.1 Day of Registration

- Patient and family caregiver will be asked to complete baseline self-report questionnaires. See Appendices II and III, respectively, for questionnaires.

7.1.2 Subsequent Medical Oncology/Infusion Visits

- A PC clinician will meet with patients randomized to early PC within one month of registration. This should be done at the patient's next medical oncology or infusion visit following registration.
- The PC clinician will meet with patients and family caregivers (if present at the appointments) at a minimum of every four weeks in the outpatient care setting (oncology clinic or infusion suite). PC visits will be coordinated with regularly scheduled cancer center appointments to reduce burden of multiple hospital visits.
- If patients are unable to come to the clinic for a scheduled PC visit, at least one attempt will be made to reschedule the visit within seven days of the scheduled PC visit. If a rescheduled in-person visit is not feasible, the PC clinician will conduct the visit over the telephone and document the content and nature of the visit in the medical record. Clinic visits are strongly preferred to telephone visits and should be attempted as much as possible.
- Patients, family caregivers, or the PC team may initiate consultations as needed.
- PC clinicians should follow the guidelines as detailed in Appendix I.
- Depending on clinic space, workflow, and patient preference, PC clinicians may see patients in the clinic or in the chemotherapy infusion room.
- If a patient is admitted to the hospital during the study period, they should be seen at least once by either their outpatient palliative care clinician or the inpatient palliative care hospital based team. Additional follow up during the hospital admission is not dictated by the study requirements and patients should be followed as per their institution practice.

7.1.3 Completion of Study Measures

Patients and family caregivers will be asked to complete quality-of-life questionnaires at weeks 6, 12, and 24. See Appendices II and III, respectively. A 2-week window, before and after each time point, for completion of the self-report questionnaires will be allowed. For example, the 12-week time point can be completed by patients and family caregivers between weeks 10 through 14.

7.2 Standard Oncology Arm

The standard oncology treatment will consist of questionnaire assessment only as outlined below.

7.2.1 Day of Registration

Patient and family caregiver will be asked to complete baseline self-report questionnaires. See Appendices II and III, respectively for questionnaires.

7.2.2 Subsequent Medical Oncology/Infusion Visits

After patients and family caregivers have been enrolled, the patient will meet with the treating oncologist(s) for the patient's standard treatment visit activities without the scheduled study intervention of palliative care.

Patients and family caregivers may consult with PC clinicians at their request or at the discretion of their treating oncologist. In such instances, individual PC clinicians will follow standard oncology participants per their clinical judgment, rather than according to the required time intervals for study patients receiving the early palliative care intervention.

7.2.3 Completion of Study Measures

Patient and family caregiver will be asked to complete self-report questionnaires at weeks 6, 12, and 24. See Appendices II and III, respectively, for questionnaires. A 2-week window, before and after each time point, for completion of the self-report questionnaires will be allowed.

7.3 Duration of Intervention

The intervention will end when the patient is deceased. Submission of patient and caregiver-provided assessments will end with the completion of week 24 assessments.

7.4 Duration of Follow-Up

Survival follow-up will be every 4 months from week 24 until death or up to 3 years (with chart abstraction at death, per section 6.4). Chart abstraction will be performed at year 1, 2, and 3 from enrollment, per section 6.4.

8.0 ADVERSE EVENTS

We do not anticipate any adverse events related to participation in this study. Based on prior experience, the study chair has enrolled over 450 patients and their family caregivers to early palliative care studies and there have been no adverse events reported for the intervention.

If patients or family caregivers experience any emotional discomfort when completing the questionnaires, they may choose not to complete them and/or speak with the site staff. Patients experiencing any physical or psychological complications as related to their standard care treatment should discuss this with their treating physician.

9.0 MEASURES

Demographics: All study participants will complete a demographic questionnaire (see Appendix III for patient, Appendix IV for family caregiver) at the time of baseline data collection detailing their age, sex, race, ethnicity, religion, relationship status, education level, annual household income, and living situation (specify number of dependent children living at home). Family caregivers will also specify their relationship with the patient, living situation (specify number of dependent children living at home) and employment status.

QOL-Patient: To assess quality of life over time in study patients, we will use the Functional Assessment of Cancer Therapy (FACT) Questionnaires, which have been validated for use in multiple care settings and with diverse tumor types. The FACT consists of four subscales assessing well-being across four domains (physical, functional, emotional and social) during the prior seven days. Additional questions specific to cancer symptoms will be added to the measure for each tumor type, including lung (FACT-L), esophageal and gastric (FACT-E), and hepatic, biliary, and pancreatic (FACT-Hep) – See Appendix III.⁵⁸⁻⁶¹ Patients will complete this questionnaire at baseline, 6, 12 and 24 weeks.

QOL-Family caregiver: We will use short-form health survey (SF-36) to assess change in health-related QOL over time in family caregivers (see Appendix IV).⁶² The SF-36 measures eight domains of health-related quality-of-life: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional health, and mental health. Family caregivers will complete this questionnaire at baseline, 6, 12 and 24 weeks.

Mood: We will use the Hospital Anxiety and Depression Scale (HADS) to assess symptoms of depression and anxiety in all study participants (see Appendix III for patient, Appendix IV for family caregiver).⁶³ The HADS is a 14-item questionnaire that contains two 7-item subscales assessing depression and anxiety symptoms during the past week. Scores on each subscale range from 0 to 21, with a cutoff of 8 or greater denoting clinically significant depression or anxiety symptoms. Patients and family caregivers will complete questionnaire at baseline, 6, 12 and 24 weeks.

Prognosis and Treatment Perceptions Questionnaire: Dr. Temel has evaluated the content validity and readability of a thirteen-item Prognosis and Treatment Perception Questionnaire (PTPQ) to assess perceptions of prognosis, goals of treatment, and quality of communication with oncologists among patients with incurable cancer (see Appendix III for patient, Appendix IV for family caregiver). The PTPQ was recently used to assess illness and prognostic understanding in patients with advanced gastrointestinal cancers.⁶⁴ We will administer the PTPQ to patients and their family caregivers in order to assess (1) illness knowledge and understanding; (2) communication and perceptions regarding prognosis and goals of care; and (3) discussions and preferences regarding EOL care. Patients and family caregivers will complete this questionnaire at 6, 12, and 24 weeks.

10.0 END OF INTERVENTION

10.1 Duration of Intervention

The patient case evaluations will continue until the patient is deceased.

10.2 Early Withdrawal

Patients and/or family caregivers may request early withdrawal from the study. Research staff will inquire regarding the reason for withdrawal and document the date and reason in the case report form. If patients assigned to the intervention arm request withdrawal due to a preference to discontinue palliative care visits, the research staff will inquire if they are still willing to complete questionnaires and allow us to access their medical records. If patients assigned to the intervention arm request withdrawal due to the questionnaires, they will still be permitted to see the palliative care clinician as per their preference. The research staff will ask for continued permission to access their medical records. Similarly, if patients assigned to the standard care arm request withdrawal due to the questionnaires, the research staff will ask for continued permission to access their medical records.

11.0 STATISTICAL CONSIDERATIONS

11.1 Study Overview

This is a randomized phase III clinical trial to determine the efficacy of early palliative care vs. standard oncology care on patient and family caregiver reported outcomes, quality of EOL care and resource utilization in newly diagnosed incurable lung or non-colorectal gastrointestinal cancer. This trial implements a group sequential design without interim analysis.

11.2 Sample Size, Accrual Time, and Study Duration

11.2.1 Sample Size

A 4-5 point change in the FACT is considered a clinically meaningful change (CMC) and was the difference detected between arms in our previous study.⁶⁵ Enrolling 140 patients per study arm will provide 80% power to detect at least a 4-point change from baseline to week 12 (standard deviation was 11.87 from the pilot study) between arms using a two-sided two-sample *t*-test with at 5% significance level.

Based on our previous palliative care study, the rate of missing data for primary endpoint patient-reported measures was approximately 20-30%. We will therefore increase our sample size to 200 patients per arm to ensure a sufficiently large margin to have adequate power to detect the CMC. Based upon our current study enrollment rates, we estimate that with 400 patients, approximately 300 family caregivers will also enroll.

11.2.2 Accrual Rate and Accrual Duration

We anticipate being able to accrue approximately 20 patients per month based on our best estimate for this new area of research. Using this estimate, we would complete accrual within 20 months and data maturation within 26 months from study initiation.

11.2.3 Primary Endpoint Completion Date for ClinicalTrials.gov Reporting

For purposes of ClinicalTrials.gov reporting, the Primary Endpoint Completion Date (PECD) for this study is the time the last patient registered has been followed for at least 12 weeks.

11.3 Statistical Design and Analysis for the Primary Endpoint

11.3.1 Primary Endpoint

The total scores of FACT-G will be calculated using the accompanying scoring algorithms. They will be further converted into a 0-100 quality of life scale for standardization. Change in FACT-G scores from baseline to 12 weeks between study arms will be the primary endpoint for this study. The disease-specific questions (additional concern) of FACT-L, FACT-E or FACT-Hep will be summarized in a descriptive manner between study arms.

11.3.2 Analysis Plan

A modified intent-to-treat principle³⁸ will be applied for statistical analysis of efficacy in evaluable patients. Evaluable patients are defined as all patients meeting the eligibility criteria who did not cancel prior to receiving intervention.

The primary analysis is to compare the change in FACT score from baseline to 12 weeks between study arms. We will perform preliminary analyses to examine how much QOL data are likely missing at random (MAR) or missing not at random (MNAR). However, missing data are expected to be MNAR as patients with poor QOL tend to have lower chances of completing a questionnaire, especially immediately prior to death.⁶⁶ We will examine the

pattern of missing data by comparing average scores among patient subsets defined by their available data and survival status. We will then use the pattern mixture models^{67,68} to adjust for MNAR bias by stratification based on survival data. We will compare study arms overall by weighting the within-stratum estimates with the estimated probability of being in each distinct combination of intervention arm and survival duration.

Sensitivity analysis will be conducted by exploring imputation method such as the last-observation carried forward, and the worst rank score analysis⁶⁹, favoring the more conservative method.

In the pattern mixture model, repeated measures of FACT will all be included in the repeated measures model to estimate the change from baseline to 12 weeks for primary analysis. Selected demographic and clinical factors (including stratification factors) may be incorporated when examining change in QOL scores across the four time points (baseline, 6, 12, and 24 weeks).

11.4 Supplementary Analysis Plans

11.4.1 Secondary Endpoints

11.4.1.1 The efficacy of early integrated palliative care (PC) on patient reported outcomes in patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer will be assessed by analyzing:

1. Change in QOL on the FACT over time
2. Rate of depressive symptoms as per HADS at 12 weeks and over time
3. Rate of anxiety symptoms as per HADS at 12 weeks and over time
4. Change in illness understanding over time

11.4.1.2 The efficacy of early integrated palliative care (PC) on family caregiver reported outcomes in those with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer will be assessed by analyzing:

1. Change in QOL on the SF-36 over time
2. Rate of depressive symptoms as per HADS at 12 weeks and over time
3. Rate of anxiety symptoms as per HADS at 12 weeks and over time
4. Change in illness understanding over time

11.4.1.3 The impact of early, integrated PC on quality of EOL care and resource utilization in patients with newly diagnosed incurable lung or non-colorectal gastrointestinal cancer will be assessed by analyzing:

1. Rate of referral, enrollment and length of stay on hospice
2. Location of death
3. Number of hospital and ICU admissions and days
4. Chemotherapy and radiation administration
5. Overall survival

11.4.1.4 Concordance between patient and family caregiver report of prognosis/curability.

11.4.2 Secondary Analysis

We will adopt the gatekeeping procedure for the primary analysis of efficacy of early PC on patient reported outcomes, the secondary analysis of efficacy of early PC on family caregiver reported outcomes, and the secondary analysis of impact of early PC on quality of EOL care and resource utilization. Therefore, they will be tested at the 5% significance level in sequence, and the subsequent analysis (hypothesis testing) will only be carried out if the previous analysis is statistically significant. Otherwise, subsequent analysis will be descriptive in nature. Multiplicity will not be adjusted for other secondary analyses, hence, statistically significant findings from secondary analyses are exploratory in nature and therefore shall be interpreted as such. Descriptive statistics and graphical approaches will form the basis for most secondary analyses.

- 11.4.2.1** To assess the changes in QOL over time among patients, generalized linear model with repeated measures will be used for comparison between treatment arms. To compare rates of psychological distress between treatment arms, we will transform the HADS score into a dichotomous outcome with categories reflecting the presence or absence of clinically significant depression and anxiety. We will then use generalized linear models with repeated measures to assess the association between the presence of depression/anxiety and study arm, using risk difference and relative risk to compare proportions between the study arms. To compare the illness understanding, we will analyze each item of the PTPQ separately using the appropriate test to determine the significance of the between-group differences. To assess additional measures of family caregiver perceptions of quality of death, we will employ the Jonckheere-Terpstra test, which is appropriate for contingency tables with ordinal data.
- 11.4.2.2** To assess the changes in QOL among family caregivers, we will use the similar approach as for QOL among patients. Change in the total score and subscales will be compared with generalized linear models with repeated measures. Analysis of psychological distress and illness understanding will be the same as above.
- 11.4.2.3** To assess differences in quality of EOL care, we will use Fisher's exact test to determine the association between the composite EOL care measure categories and study arm and a comparison of rates between the groups based on the risk difference and relative risk. To assess the difference in resource utilization, we will also compare days on hospice and in the hospital and ICU using the Mann-Whitney U test. To compare patient survival, we will use Kaplan-Meier estimates, testing the difference between the curves with the log-rank test.
- 11.4.2.4** To assess the concordance between patient and family caregiver report of prognosis/curability, we will analyze each of the primary and secondary endpoints using the matched-pair subset. Simple tests such as paired *t*-test, Wilcoxon signed-rank test, and generalized linear models for matched pair data will be utilized.

11.5 Study Monitoring

11.5.1 Adverse Event Stopping Rule

Not applicable.

11.5.2 Accrual Monitoring Stopping Rule

Slow Accrual: Patient accrual will be closely monitored by the investigators and secondary statistician on a monthly basis. If the accrual rate falls below 50% of expected accrual rate, investigators will carefully review feedback from sites and consider taking measures to encourage patient enrollment.

11.5.3 Community vs Academic Accrual

The NCI has requested that at least half the patients enrolled on this study be accrued from community centers. Therefore, patient accrual will be monitored by community vs academic accrual. If the accrual target for academic is met, we may limit future patient accrual to community sites only.

11.6 Study Reporting

11.6.1 This study will be monitored by the Alliance Data Safety Monitoring Board (DSMB), an NCI-approved functioning body. Reports containing efficacy, adverse event, and administrative information will be provided to the DSMB every month as per NCI guidelines.

11.6.2 Results Reporting on ClinicalTrials.gov: At study activation, this study will have been registered within the “ClinicalTrials.gov” web site. The Primary and Secondary Endpoints (i.e., “Outcome Measures”) along with other required information for this study will be reported on ClinicalTrials.gov.

11.7 Descriptive Factors

None.

11.8 Inclusion of Women and Minorities

This study will be available to all eligible patients, regardless of race, gender, or ethnic origin. There is no information currently available regarding differential effects of this intervention in subsets defined by race, gender, or ethnicity, and there is no reason to expect such differences to exist. Therefore, although the planned analysis will, as always, look for differences in treatment effect based on racial and gender groupings, the sample size is not increased in order to provide additional power for subset analyses.

The geographical region served by the Alliance includes approximately 13.5% minorities. Based on prior Alliance studies involving similar disease sites, we expect about 11.6% of patients will be classified as minorities by race and about 60% of patients will be women. Expected sizes of race by gender subsets for patients randomized to this study are shown in the following table.

Racial Categories	Ethnic Categories					
	Not Hispanic or Latino		Hispanic or Latino			
	Female	Male	Female	Male		
American Indian/ Alaska Native	2	1	0	0	3	
Asian	4	3	0	0	7	
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	
Black or African American	20	16	0	0	36	
White	209	137	5	3	354	
More Than One Race	0	0	0	0	0	
Total	235	157	5	3	400	

12.0 GENERAL REGULATORY CONSIDERATIONS AND CREDENTIALING

12.1 Institutional Palliative Care Requirements

The requirements for the PC teams at participating Alliance sites are as follows:

- Sites must have the capacity to perform visits at the cancer practice.
- PC service must have the ability to see patients on the same days as their oncology visits (clinic, radiation, or chemotherapy).
- The PC clinic must have a minimum of six months of experience of providing care in the outpatient setting.
- The outpatient PC service must be led by a board certified palliative care physician or advanced practice nurse.
- If patients randomized to the PC study arm are admitted to hospitals with an inpatient PC team, they must be followed by that inpatient PC team.
- At least one lead member of the PC outpatient team must be willing to complete two 1-hour web-based training courses and review the protocol intervention manual and use this information to train the rest of the palliative care team that is participating in this trial.
- At least one lead member of the PC outpatient team must be willing to participate in periodic PC teleconferences (no more frequently than monthly) with [REDACTED].

12.2 Individual Palliative Care Credentialing

The requirements for the PC teams at participating Alliance sites are as follows:

- The physician or advanced practice nurse PC leader for this study must be board certified.
- Leader must provide verification of completion of both A221303 web-based training courses.
- Palliative care provider must have read 'Early Integration of Palliative and Oncology Care: An Intervention Manual' in Appendix I.

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14.0 MODEL CONSENT FORMS

Patient Model Consent

Testing the addition of early palliative care to usual cancer care in patients with incurable lung or non-colorectal gastrointestinal cancers

Official Study Title for Internet Search on <http://www.ClinicalTrials.gov>: (Randomized Study of Early Palliative Care Integrated with Standard Oncology Care versus Standard Oncology Care Alone in Patients with Incurable Lung or Non-Colorectal Gastrointestinal Malignancies)

What is the usual approach to my incurable lung or non-colorectal gastrointestinal cancer?
You are being asked to take part in this study because you have incurable lung or non-colorectal gastrointestinal cancer. When patients are diagnosed with advanced cancer, their oncology doctors and nurses usually provide most of their care. At a later time, when their disease worsens and they develop more symptoms, they may also be referred to doctors and nurses who specialize in palliative care.

If you are not familiar with the term “palliative care”, this refers to doctors and nurses who specialize in the lessening (“palliation”) of symptoms associated with cancer. Palliative care focuses on improving the quality of life for patients with advanced diseases and their family members by providing support for relief of physical symptoms, emotional and psychological support, and counseling.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach to your cancer care
- you may choose to take part in a different study, if one is available
- you may choose to discuss palliative care at any time with your doctor in addition to having your usual cancer care without participating in this study.

Why is this study being done?

Patients with advanced cancer often feel stress and worry and have symptoms such as fatigue or pain. The purpose of this study is to see whether patients who receive care from palliative care doctors and nurses at an earlier time in their disease, along with their regular cancer care, will experience less emotional and physical issues from their cancer.

The effects of the early involvement of the palliative care team will be compared to the usual approach of receiving care mostly from the cancer treatment team (as described in the beginning of this consent form).

There will be about 400 patients enrolled in this intervention study and there will be about 300 family caregivers enrolled as well.

What are the study groups?

This study has two study groups. Group 1 will receive early palliative care in addition to their usual cancer care and Group 2 will receive their usual cancer care.

A computer will by chance assign you to one of the two groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.

How long will I be in this study?

You will be on this study for as long as you receive care for your disease.

What extra tests and procedures will I have if I take part in this study?

There are no extra exams, tests, or procedures that you will need to have if you take part in this study, with the exception of completing questionnaires. If you are seeing the palliative care team in addition to your usual cancer care, the palliative care team will try to have their visits with you when you are at the cancer center for your regular cancer care or treatment. If the palliative care team cannot see you when you attend regular doctor visits for cancer care or treatment, they may schedule their visit with you on another day.

You will be asked to complete a packet of questions when you start the study and in 6, 12 and 24 weeks when you come for your regular cancer care visits. These questions will ask about some personal information (such as your ethnicity), about how you are feeling (including symptoms like fatigue or sadness), and about what you understand about your diagnosis and planned treatment. The questionnaire should take about 15-20 minutes to complete each time.

We will also ask your family caregiver to complete a packet of questionnaire when you start the study and in 6, 12, and 24 weeks.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may be asked sensitive or private questions in the study question packet. If you feel uncomfortable about answering any questions, you do not have to answer them.

Let your study doctor know of any questions or concerns you may have about the study question packet. You can ask the study doctor about these questions at any time.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the early palliative care in addition to usual cancer care approach is better than the usual cancer care approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, Institutional Review Board or Food and Drug Administration.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ (insert name of center) Institutional Review Board at _____ (insert telephone number). *(Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

The palliative care team visits will be billed to your health plan/insurance company. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

What happens if I am injured or hurt because I took part in this study?

You are not expected to have a physical injury related to this study.

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The Alliance for Clinical Trials in Oncology
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

You may visit the NCI Web site at <http://cancer.gov/> for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ (*insert name of study doctor[s]*) at _____ (*insert telephone number*).

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, _____, (*insert name of study doctor for main trial*), at _____ (*insert telephone number of study doctor for main trial*).

My Signature Agreeing to Take Part in the Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study.

Participant's signature _____

Date of signature _____

Signature of person(s) conducting the informed consent discussion _____

Date of signature _____

Family Caregiver Model Consent

Testing the addition of early palliative care to usual cancer care in patients with incurable lung or non-colorectal gastrointestinal cancers

You are being asked to take part in a research study about how the treatment of a friend or family member who has incurable lung or non-colorectal gastrointestinal cancer has affected your everyday life. You are being asked to participate in this study because your friend or family member has agreed to participate in this study to determine whether having patients get palliative care at an earlier time in their disease treatment along with their regular cancer care will improve the emotional and physical issues related to having cancer.

If you are not familiar with the term “palliative care”, this specialty refers to health care clinicians who specialize in the lessening (“palliation”) of disease symptoms. Palliative care focuses on improving the quality of life for patients with advanced diseases and their family members by providing support for relief of physical symptoms, emotional and psychological support, and counseling.

Participation in this study is purely voluntary. Your decision to participate will not affect your friend or family member's ability to receive medical care in any way.

There will be about 400 patients enrolled in this intervention study and about 300 friend or family caregivers enrolled. If you should accept our invitation to participate in this study, we would like to ask you questions about how your significant other's having cancer has affected you emotionally and physically, as well as your everyday activities, family and social life, and finances. You will be asked to complete questionnaires at four time points – shortly after you sign this consent form, and at 6, 12, and 24 weeks. These questions will ask about some personal information, such as, about how you are feeling and about your understanding of your friend or family member's disease and planned treatment. Completing the questionnaires will take approximately 15-20 minutes each, and will be done at a time during your friend or family member's regular cancer care visits, at no cost to you. The answers that you give to the interviewer will be confidential, meaning that your answers will not be shared with your significant other or members of his/her medical team. If your friend or family member decides not to take part in this study at any time, it will also end your participation in this study. Your participation in this study will help us better understand how early palliative care intervention affects how cancer patients are feeling and whether it improves their quality of life. Please sign below if you agree to complete the questionnaires described in this document at the indicated time points. We thank you for your cooperation.

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in this study.

(Participant's Signature)

(Date)

(Name of Responsible Investigator)

(Phone #)

APPENDIX I: EARLY INTEGRATION OF PALLIATIVE & ONCOLOGY CARE: A TREATMENT MANUAL

**Early Integration of Palliative and Oncology
Care: An Intervention Manual**

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Early Palliative Care Intervention Manual

Background

Palliative care represents a specialty-trained medical discipline that focuses on enhancing quality-of-life, symptom management, coping, treatment decision-making as well as psychosocial and spiritual support for patients with serious illnesses and their family caregivers. Often consisting of physicians, nurses, social workers, and chaplains, the multidisciplinary palliative care team primarily aims to help patients with medical illness live as well as possible for as long as possible. However, historically, patients and families have received such services late in the course of disease in the inpatient setting as consultations for uncontrolled symptoms or for planning end-of-life care.

New evidence from several trials suggest that patients with advanced cancer who receive palliative care services from the time of diagnosis experience a number of beneficial clinical outcomes, such as better quality-of-life, lower rates of depression, more accurate prognostic awareness, and higher quality end-of-life care. In a comprehensive review of the literature, Greer and colleagues (2013) have documented the rationale and evidence base for early palliative care for patients with advanced cancer. Given these positive results, national professional organizations such as the American Society of Clinical Oncology, have recommended consideration of referral to palliative care early in the course of disease for patients diagnosed with metastatic cancer.

The integration of palliative care and standard oncology care in the outpatient setting includes unique features of practice that are distinct from the traditional model of inpatient palliative care. To ascertain the components of early palliative care, we have gathered data from multiple sources including: 1) chart review, 2) focus group interviews with palliative care clinicians, and 3) qualitative analyses of audio-recordings of early palliative care consultations for patients diagnosed with metastatic lung or advanced non-colorectal gastrointestinal cancers. Based on these data sources, we have outlined the following six domains of early palliative care:

- Developing and maintaining the **therapeutic relationship** with patients and family caregivers
- Assessing and treating **patient symptoms**
- Providing support and reinforcement of **coping with advanced cancer** in patients and family caregivers
- Assessing and enhancing **prognostic awareness and illness understanding** in patients and family caregivers
- Assisting with **treatment decision-making**
- Planning for **end-of-life care**

In the following treatment manual, we detail the essential content and processes of the aforementioned early palliative care domains, in order to facilitate clinician education and dissemination of such services. Although the content domains of early palliative care often occur across multiple sessions or several may occur within a single consultation, we will present the information according to the types of palliative care interventions that occur most prominently during the following time frames: at initiation of treatment; throughout the entire course of disease; at clinical turning points (e.g., changing to a new regimen of chemotherapy or after being discharged from the hospital); and upon the conclusion of outpatient treatment and/or transition to hospice services.

Initial Outpatient Palliative Care Visits in the Oncology Setting

Key Domain: Therapeutic Relationship

Although developing and maintaining the therapeutic relationship is essential across all palliative care visits throughout the course of disease, the prominent focus of initial consultations soon after diagnosis in the outpatient setting is rapport building and establishing trust.

- Introducing Palliative Care: The primary focus of the early palliative care consultation soon after

diagnosis involves the development of a strong therapeutic relationship and rapport building with patients and family caregivers. In the context of a new cancer diagnosis for patients with incurable disease, the referral to palliative care works best if the oncologist either personally introduces the palliative care clinician during a joint visit or discusses the value of the palliative care team and collaborative nature of treatment to support the patient and family.

- The PC clinician will often begin the first consultation by eliciting the patient's and family caregiver's understanding of palliative care, ideally to identify their baseline knowledge and familiarity with the service as well as to debunk any myths about the treatment.
- To help reduce potential resistance, the PC clinician will then emphasize the role of palliative care to help the patient and family caregivers achieve the best possible quality-of-life through expert symptom management, support, and assistance with treatment decision-making.
- The PC clinician explains the nature of the service as a multidisciplinary team that is available to the patient and family caregiver throughout the disease process. This conversation may also need to differentiate early outpatient palliative care from hospice care.
- Understanding the Patient and Family Caregiver Experience: A key feature of building rapport is learning about the values, life goals, and experiences of patients and their family caregivers both prior to and after the cancer diagnosis. The PC clinician can accomplish this by asking about the following areas:
 - The patient's life experiences outside the context of disease (including work, family, hobbies/interests, spiritual or religious involvement, etc.)
 - Lifestyle changes that have resulted from the diagnosis and treatment of cancer
 - Patients' and family caregivers' current wishes, priorities, and emotions, while providing validation
- Building Trust with the Patient and Family Caregiver: PC clinicians develop trust and credibility with patients and family caregivers by outlining the parameters of communication and providing reassurance. For example, the following strategies help facilitate trust:
 - Acknowledging the role of the PC clinician in helping the patient to "live as well as possible for as long as possible."
 - Clarifying and validating what the patient wishes and does not wish to discuss
 - Encouraging the patient to disclose symptoms and other concerns to the PC clinician
 - Reinforcing the partnership between the patient and family caregiver and PC clinician
 - Reassuring the patient and family caregiver that discussions about end-of-life care or other medical decisions will be raised when necessary.

Outpatient Palliative Care Visits throughout the Entire Course of Disease

Key Domain: Patient Symptoms

Based on our review of early PC consultations, symptom management is a prominent focus of all palliative care visits from initial consultation and throughout the course of disease. Assessing and treating symptoms to enhance quality-of-life is one of the primary ways that PC clinicians establish trust and credibility with patients and family caregivers. In this way, PC clinicians demonstrate the collaborative nature of integrated palliative and oncology care.

- Preparing for Symptoms: Patients and families often experience concern about the trajectory of illness and treatment side effects. PC clinicians in the outpatient setting provide an invaluable service by clarifying the likely symptoms patients will experience, while offering reassurance about the methods for reporting and treating such symptoms as they occur. PC clinicians will

want to explain their role and availability for symptom management both during and between clinic visits.

- Assessing and Treating Symptoms: At every consultation, the PC clinician will conduct a review of systems to elicit existing and new symptom concerns, especially as related to disease and treatment side effects.
 - The common symptoms patients with incurable cancer will report in the outpatient setting include: pain, dyspnea/cough, fatigue, gastrointestinal symptoms, neurologic symptoms, edema, mood/emotional symptoms, sleep-related symptoms, issues of sexuality, and other symptoms including pre-existing or co-morbid conditions.
 - Our review of PC consultations for patients with incurable lung or non-colorectal GI cancers revealed that while symptoms can be quite variable per individual patient, pain and fatigue are frequently reported across all palliative care visits. Also, PC clinicians note that they treat nausea/vomiting more often with transitions in chemotherapy, whereas dyspnea and anxiety symptoms occur more frequently later, such as after hospitalization and referral to hospice care.
 - PC clinicians draw on their expert training and skill in medical management of complex symptom clusters with use of opioids, non-opioid analgesics, anti-emetic agents, and psychotropic agents, etc.
- Coordinating Symptom Management with Oncology: When working closely with the oncologist, the PC clinician will need to maintain ongoing, effective communication with the treatment team to define this mutual collaboration and work within the preferred practice patterns of individual oncologists. Specifically, some oncology clinicians may want to take a more or less active role in managing symptoms. Thus, PC clinicians provide an extra layer of support for both the oncology team and patient.
- Providing Referral for Symptom Management: Although PC clinicians possess expertise to assess and treat severe and poorly controlled symptoms, they also emphasize the team approach to comprehensive cancer care by referring to specialty care, mental health (e.g., psychiatry, psychology, social work), alternative medicine (e.g., acupuncture, massage, art therapy), and spiritual support as needed.

Key Domain: Coping with Advanced Cancer

As in the case of symptom management, early PC clinicians address how patients and family caregivers are coping with advanced cancer across clinic visits throughout the course of disease. The provision of early palliative care affords the opportunity and time for counseling patients and family caregivers to enhance adjustment and coping with the many existential and lifestyle changes that occur as a result of cancer and its treatment. In particular, the aim is to help patients maintain hope and engagement with life activities to the extent that is possible and consistent with their functioning.

- Reviewing and Validating Prior Coping Efforts: PC clinicians value and recognize that patients and family caregivers bring their own expertise in coping to the current circumstance based on how they have managed difficulties and crises in the past.
 - The PC clinician often begins the discussion of coping by asking patients and family caregivers what strategies (e.g., use of social support, seeking counseling, increasing self-care activities, etc.) they have used to adjust to other life transitions or losses. During this conversation, the PC clinician strives to highlight and reinforce all adaptive forms of coping, while also assessing for potentially harmful behaviors (e.g., substance use, social withdrawal, etc.).
 - While it is natural in times of crisis to doubt one's capacity to cope, the PC clinician

communicates to patients and family caregivers that they have the strength and abilities to meet their imminent challenges by highlighting successful prior coping efforts. Moreover, by emphasizing the partnership with the treatment team, the PC clinician reinforces that patients and family caregivers are not alone as they navigate the many treatments, scans, symptoms, and uncertainties of related to advanced cancer.

- Discussing and Advocating for Different Methods of Coping: After assessing and validating prior coping, PC clinicians also introduce various strategies and approaches to help improve adjustment and meaning in life. For example, the following topics may be explored:
 - Behavioral approaches: Specifically, PC clinicians may employ evidence-based techniques for stress reduction (e.g., breathing and relaxation exercises); behavioral activation (remaining engaged with important activities and sustaining normal life as much as possible even with the disease); sleep hygiene; exercise; and activity pacing as needed due to pain, fatigue or other symptoms.
 - Spiritual approaches: PC clinicians assess the role that spirituality plays in a patient's life in a respectful and non-judgmental manner and with a broad perspective to incorporate multiple meanings of spirituality (such as religious affiliation and participation in community of faith, personal spiritual beliefs and practices, cultural traditions, etc.).
 - Accepting Illness while Maintaining Hope: PC clinicians help patients and family caregivers understand that acceptance of illness has cognitive, behavioral, and emotional elements. For example, although patients may more or less intellectually understand their prognosis and course of disease, they often experience difficulty in emotionally processing this information. By offering a safe venue for patients and family caregivers to ask questions about the disease, clarify uncertainties, and experience the related affect, PC clinicians facilitate cognitive and emotional acceptance of illness. Also, PC clinicians help patients and family caregivers achieve behavioral acceptance by defining the parameters of what is their control, acknowledging the limitations due to disease, and maintaining hope for achieving valued quality-of-life goals.
- Social Support: PC clinicians help patients and family caregivers define the different forms of social support they need, such as pragmatic versus emotional support. In other words, they clarify which individuals help with making meals, transportation to appointments, going shopping etc., as well as those who are available to listen and offer emotional support for discussing the experience of life-limiting cancer. Also, the PC clinician works with patients and families to identify any gaps and problem-solve strategies for soliciting needed support. Conducting Life Review: Although not all patients will have the interest or capacity to reflect on their life experiences in a meaningful way, some will appreciate the process of life review as a form of existential coping. Specifically, as patients approach the end-of-life, some seek to take time to reflect on their life story and experiences, consider their legacy, and explore how they want to spend their remaining time. Such life review work might also include specific activities such as writing letters to loved ones, completing unfinished tasks, reconciling relationships with family and friends, completing a creative or artistic project (e.g., scrapbook, personal history, quilt, woodworking, etc.), as a representation of who the patient is and expression of love for others.
- Supporting Family Caregiver Coping: Research shows that patient distress is highly related to family caregiver distress and vice versa. In the early palliative care setting, PC clinicians have the rare opportunity to bolster family caregiver coping by conducting ongoing assessments of burden, enhancing communication between patients and loved ones, and providing recommendations for additional support or referral.
- Referring for Additional Support: Again, the PC clinician calls upon other members of the

supportive care team as needed for patients and family caregivers who may be experiencing complicated or severe distress. Referrals to social work, psychology, psychiatry, and pastoral care may be useful depending on the specific presenting circumstances and concerns.

Outpatient Palliative Care Visits during Clinical Turning Points

Key Domain: Prognostic Awareness and Illness Understanding

Based on our review of early PC consultations during clinical turning points, such as starting a new chemotherapy regimen or after hospitalization, symptom management and coping with illness remain prominent foci of treatment. However, PC clinicians also report with increased frequency discussions about illness understanding and treatment decision-making. Of note, the assessment and discussion of prognosis and illness understanding is not a single event but rather occurs over multiple visits, a benefit of the longer relationship that early PC clinicians develop in the outpatient setting.

- Communication with Oncologist: The PC clinician must first consult with the primary oncologist to ensure the care team is consistent with their understanding of patient prognosis before engaging in detailed communication with the patient about the likely course of disease. When possible, joint clinic visits between oncology and palliative care will reinforce the team approach to care and ensure clear and effective communication with patients and family caregivers.
- Assessing and Informing Patient Expectations of Prognosis and Illness Process: We require reading the article by Jackson et al. (2013), which provides a detailed account of how to cultivate prognostic awareness and deliver information about the disease process of advanced cancer in the early palliative care setting. By way of summary, PC clinicians recognize that patient and family caregiver illness understanding often vacillates between more and less realistic expectations over time, or even within the same clinic visit, which can be confusing for clinicians. The following strategies help improve prognostic awareness in a manner that is consistent with the degree of cognitive-emotional coping and acceptance observed in patients and family caregivers.
 - Assessment of prognostic awareness begins with asking patients and family caregivers in an open- ended manner about their understanding of the disease and their future. The responses from patients provide some clarity about the level of awareness and also their ability to tolerate discussions regarding prognosis. For patients who struggle to have these conversations, framing questions with the hypothetical of “imagining a poorer health state” may be useful.
 - Communication strategies for delivering prognostic information include the “Ask-Tell-Ask” and “Pairing Hope with Worry” techniques (for further details, see Jackson et al., 2013). PC clinicians understand that they must clarify the type of information patients and family caregivers want to know, such as questions about expected length of life versus concerns about how the disease changes over time and what the dying process is like.
 - As patients and family caregivers begin to understand and integrate information about prognosis, they will often experience heightened affect such as disbelief, sadness, anger, etc. Rather than blocking or providing false reassurance, the PC clinician’s role is to witness and validate these emotions with silence, an empathic touch, re-statement of realistic hopes, and “I wish” statements (e.g., *“It sounds like that was hard to hear. I wish I had better news.”*)
 - The PC clinician can then pivot to discuss again those aspects of care and the disease that can be controlled, emphasizing realistic hopes and quality-of-life goals (e.g., helping patient to feel well enough to spend valuable time with grandchildren).
- Conducting Separate Conversations with Family Caregivers about Illness Understanding: The

vacillation in patients' prognostic awareness over time is not only challenging for clinicians but can also be difficult for family caregivers. Ideally, conversations about prognosis and illness understanding occur with both patients and family caregivers present, though this may not always be possible or clinically appropriate. In such circumstances, the PC clinician obtains consent from the patient to discuss illness concerns separately with identified family caregivers. Such conversations can help family caregivers understand the process of illness understanding, including the normal pattern of vacillation between more and less accurate prognostic awareness, offering strategies for communication and support.

Key Domain: Treatment Decision-making

As noted earlier, although discussion of treatment decision-making can occur at any point along the illness trajectory for patients with advanced cancer, early PC clinicians report more frequent discussions of this topic during times of clinical transitions, such as when starting or stopping chemotherapy or initiating hospice services.

- Assessing Patient Values in Treatment Decision-making: In the shared decision-making process about cancer care, the early PC clinician elicits information from patients and family caregivers regarding their decision-making style, quality versus quantity of life concerns, and life goals. The aim of this assessment is to determine the extent to which patient's preferences and values align with current or potential treatments.
- Discussing Treatment Considerations: Given their medical expertise, early PC clinicians provide an extra layer of support for patients and family caregivers to understand the efficacy, risks and benefits, side effects, and potential burdens associated with different forms of cancer treatment. Furthermore, these conversations provide an opportunity to reinforce the role of palliative care for mitigating symptoms and toxicities.
- Supporting Treatment Decisions: PC clinicians value and reinforce patient autonomy in making informed treatment decisions. At multiple points during the course of cancer care, patients must discern whether to start, continue, or stop treatments in collaboration with their cancer care team, as well as decide the extent to which family caregivers are consulted about these decisions. In this context, early PC clinicians help clarify any misunderstanding about treatment, support patient decision-making and freedom to change course, as well as facilitate communication with family caregivers and members of the oncology team.

Final Outpatient Palliative Care Visits and Transition to Hospice Services

Key Domain: End-of-Life Care

Based on our review of early PC consultations, PC clinicians generally raise the discussion of end-of-life (EOL) care incrementally over time and most prominently later in the course of illness, after having established a strong, trusting therapeutic relationship with patients and family caregivers. Typically, the final palliative care visits in the outpatient setting focus not only on symptom management, illness understanding, and decisions about stopping cancer therapy but also on advance care planning.

- Discussing End-of-Life Care Options: Given the longer length of the clinical relationship with early palliative care, PC clinicians have the advantage to reduce patient anxiety in discussing EOL care concerns by having such conversations in a piecemeal fashion over time. The primary topics for EOL care planning include discussions regarding: selection of healthcare proxy, determination of resuscitation preferences, will/estate planning, hospice care, location of death, and funeral planning.
- Supporting Family caregivers in EOL Care Coordination and Bereavement: Most patients with advanced cancer will experience progressive decline in their functional status over time. Thus,

they often require additional assistance from family and loved ones for personal care and communication of their values and wishes as they approach the end-of-life. This caregiving role can be both personally meaningful and stressful for family members and loved ones.

- The PC clinician works closely with patients and family caregivers to determine the available resources for EOL care and whether it is appropriate for patients to receive their terminal care in the home or other hospice or inpatient settings. PC clinicians can also serve as advocates for family caregivers in making plans for the will/estate and funeral.
- Early PC clinicians recognize that their specialized care considers the family unit as the focus of treatment. As such, they continue to provide resources, support, counseling, and referral for bereavement in family caregivers after the patient has died.

Conclusion

Our intent in developing this treatment manual is to support palliative care clinicians in the outpatient setting who provide care for patients with advanced cancer and their families. While the manual offers an organizational framework and highlights the essential components and processes of early palliative care, we recognize the value of the PC clinicians' clinical judgment in discerning the appropriate timing and exact tailoring of these interventions for delivery in a patient-centered manner.

Highly Recommended Readings:

1. Jackson VA, Jacobsen J, Greer JA, et al: The cultivation of prognostic awareness through the provision of early palliative care in the ambulatory setting: a communication guide. *J Palliat Med* 16:894-900, 2013
2. Jacobsen J, Thomas J, Jackson VA. Misunderstandings about prognosis: an approach for palliative care consultants when the patient does not seem to understand what was said. *J Palliat Med*. 2013 Jan;16(1):91-95.
3. Jacobsen J, Kvale E, Rabow M, Rinaldi S, Cohen S, Weissman D, Jackson V. Helping Patients with Serious Illness Live Well through the Promotion of Adaptive Coping: A Report from the Improving Outpatient Palliative Care (IPAL-OP) Initiative. *J Palliat Med*. 2014 Feb; 17 (4):1-6.

Additional Recommended Readings:

1. Greer JA, Jackson VA, Meier DE, et al: Early integration of palliative care services with standard oncology care for patients with advanced cancer. *CA Cancer J Clin* 63:349-63, 2013
2. Greer JA, Pirl WF, Jackson VA, et al: Effect of early palliative care on chemotherapy use and end- of-life care in patients with metastatic non-small-cell lung cancer. *J Clin Oncol* 30:394-400, 2012
3. Jacobsen J, Jackson V, Dahlin C, et al: Components of early outpatient palliative care consultation in patients with metastatic nonsmall cell lung cancer. *J Palliat Med* 14:459-64, 2011
4. Temel JS, Greer JA, Muzikansky A, et al: Early palliative care for patients with metastatic non- small-cell lung cancer. *N Engl J Med* 363:733-42, 2010
5. Temel JS, Greer JA, Admane S, et al: Longitudinal perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer: results of a randomized study of early palliative care. *J Clin Oncol* 29:2319-26, 2011
6. Yoong J, Park ER, Greer JA, et al: Early palliative care in advanced lung cancer: a qualitative study. *JAMA Intern Med* 173:283-90, 2013

APPENDIX II: PATIENT AND CAREGIVER INFORMATION SHEETS

PATIENT INFORMATION SHEET

**Patient Completed Booklet
(Baseline)**

You have been given a booklet to complete for this study visit. The booklet contains some questions about your 'quality-of-life' as a patient receiving treatment for cancer. Your answers will help us to better understand how the treatment you are receiving is affecting the way you feel.

1. You are being asked to complete a questionnaire booklet for this study. This booklet must be completed on the day you enroll in the study.
 - a. This booklet contains of the following questionnaires:
 - Demographics
 - FACT-L Questionnaire (as applicable to your disease)
 - Hospital Anxiety and Depression Scale
2. Directions on how to complete each set of questions are written on the top of each set.
3. It is very important that you return the booklets to us, whether you finish the study or not.
4. You will be given the nurse's or study coordinator's name and telephone number. You can call anytime with any concerns or questions.
5. After completing this booklet, please return it to your nurse or physician at your next visit or mail it back in the provided envelope.

Thank you for taking the time to help us.

PATIENT INFORMATION SHEET
Patient Completed Booklet
(Baseline)

You have been given a booklet to complete for this study visit. The booklet contains some questions about your 'quality-of-life' as a patient receiving treatment for cancer. Your answers will help us to better understand how the treatment you are receiving is affecting the way you feel.

1. You are being asked to complete a questionnaire booklet for this study. This booklet must be completed on the day you enroll in the study.
 - a. This booklet contained 3 sets of questions:
 - Demographics
 - FACT-E Questionnaire (as applicable to your disease)
 - Hospital Anxiety and Depression Scale
2. Directions on how to complete each set of questions are written on the top of each set.
3. It is very important that you return the booklets to us, whether you finish the study or not.
4. You will be given the nurse's or study coordinator's name and telephone number. You can call anytime with any concerns or questions.
5. After completing this booklet, please return it to your nurse or physician at your next visit or mail it back in the provided envelope.

Thank you for taking the time to help us.

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(Baseline)

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1. You are being asked to complete a questionnaire booklet for this study. This booklet must be completed on the day you enroll in the study.
 - a. This booklet contained 3 sets of questions:
 - Demographics
 - FACT-Hep Questionnaire (as applicable to your disease)
 - Hospital Anxiety and Depression Scale
2. Directions on how to complete each set of questions are written on the top of each set.
3. It is very important that you return the booklets to us, whether you finish the study or not.
4. You will be given the nurse's or study coordinator's name and telephone number. You can call anytime with any concerns or questions.
5. After completing this booklet, please return it to your nurse or physician at your next visit or mail it back in the provided envelope.

Thank you for taking the time to help us.

PATIENT INFORMATION SHEET
Patient Completed Booklet
(6, 12, and 24 Weeks)

You have been given a booklet to complete for this study visit. The booklet contains some questions about your 'quality-of-life' as a patient receiving treatment for cancer. Your answers will help us to better understand how the treatment you are receiving is affecting the way you feel.

1. You are being asked to complete a questionnaire booklet for this study for the following time points:
 - 6 weeks after your first study visit
 - 12 weeks after your first study visit
 - 24 weeks after your first study visit
 - a. Each booklet contains the following questionnaires:
 - FACT-L Questionnaire (as applicable to your disease)
 - Hospital Anxiety and Depression Scale
 - Prognosis and Treatment Perceptions Questionnaire
2. Directions on how to complete each set of questions are written on the top of each set.
3. It is very important that you return the booklets to us, whether you finish the study or not.
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Thank you for taking the time to help us.

PATIENT INFORMATION SHEET
Patient Completed Booklet
(6, 12, and 24 Weeks)

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 - 6 weeks after your first study visit
 - 12 weeks after your first study visit
 - 24 weeks after your first study visit
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 - FACT-E Questionnaire (as applicable to your disease)
 - Hospital Anxiety and Depression Scale
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(6, 12, and 24 Weeks)

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 - 6 weeks after your first study visit
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- a. Each booklet contains the following questionnaires:
 - FACT-Hep Questionnaire (as applicable to your disease)
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5. After completing this booklet, please return it to your nurse or physician at your next visit or mail it back in the provided envelope.

Thank you for taking the time to help us.

FAMILY CAREGIVER INFORMATION SHEET
Family Caregiver Completed Booklet
(Baseline)

You have been given a booklet to complete for this study visit. The booklet contains some questions about your 'quality-of-life' as a family caregiver of a patient with cancer. Your answers will help us to better understand how caring for a patient with cancer is affecting the way you feel.

1. You are being asked to complete a questionnaire booklet for this study. This booklet must be completed on the day you enroll in the study.
 - a. This booklet contains the following questionnaires:
 - Demographics
 - Short Form-36
 - Hospital Anxiety and Depression Scale
2. Directions on how to complete each set of questions are written on the top of each set.
3. It is very important that you return the booklets to us, whether you finish the study or not.
4. You will be given the nurse's or study coordinator's name and telephone number. You can call anytime with any concerns or questions.
5. After completing this booklet, please return it to your nurse or physician at your next visit or mail it back in the provided envelope.

Thank you for taking the time to help us.

FAMILY CAREGIVER INFORMATION SHEET
Family Caregiver Completed Booklet
(6, 12, and 24 Weeks)

You have been given a booklet to complete for this study visit. The booklet contains some questions about your 'quality-of-life' as a family caregiver of a patient with cancer. Your answers will help us to better understand how caring for a patient with cancer is affecting the way you feel.

1. You are being asked to complete a questionnaire booklet for this study for the following time points:
 - 6 weeks after your first study visit
 - 12 weeks after your first study visit
 - 24 weeks after your first study visit
 - a. Each booklet contains the following questionnaires:
 - Short Form-36
 - Hospital Anxiety and Depression Scale
 - Prognosis and Treatment Perceptions Questionnaire
2. Directions on how to complete each set of questions are written on the top of each set.
3. It is very important that you return the booklets to us, whether you finish the study or not.
4. You will be given the nurse's or study coordinator's name and telephone number. You can call anytime with any concerns or questions
5. After completing this booklet, please return it to your nurse or physician at your next visit or mail it back in the provided envelope

Thank you for taking the time to help us.

APPENDIX III: PATIENT REPORTED MEASURES

Patient Demographics Form

Please check the appropriate box or boxes.

Age ____

1. Race (Mark one with an X.)

(Choose the race which most accurately describes you.)

- American Indian or Alaskan Native
- Asian
- Black or African American
- Native Hawaiian or other Pacific Islander
- White
- Not reported
- Unknown

2. Ethnicity (Mark one with an X.)

- Hispanic or Latino
- Not Hispanic or Latino
- Not reported
- Unknown

3. Religion (Mark one with an X.)

- Catholic
- Protestant
- Jewish
- Muslim
- None
- Unknown
- Not reported
- Other (specify) _____

4. What is your marital status? (Mark one with an X.)

- Married
- Domestic partnership
- Widowed
- Divorced
- Separated
- Never married
- I prefer not to answer
- Unknown/Not reported

5. What is the highest grade you finished in school? (Mark one with an X.)

- 8th grade or less
- 9th-11th grade
- High school graduate/GED
- Associate degree/some college
- Vocational/technical school
- Bachelor's degree
- Advanced degree
- I prefer not to answer

6. What was the total combined income of your household in the past year, including income from all sources such as wages, salaries, Social Security or retirement benefits, help from relatives and so forth? Please tell us the total income before taxes. (Mark one with an X.)

- Less than \$20,000
- \$20,000 – \$49,999
- \$50,000 – \$89,999
- \$90,000 – \$119,999
- \$120,000 or above
- Unknown
- I prefer not to answer

7. With whom do you live? (Mark all that apply with an X.)

- Spouse/partner
- Girlfriend/boyfriend
- Children aged 18 years or younger
- Children aged 19 years or older
- Parent(s)/parent(s)-in-law
- Live alone
- Other (specify) _____
- Other relative (specify) _____

Hospital Anxiety and Depression Scale

Name:

Date:

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he will be able to help you more.

This questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought-out response.

Tick only one box in each section

I feel tense or 'wound up':

Most of the time.....
A lot of the time.....
Time to time, Occasionally.....
Not at all.....

I feel as if I am slowed down:

Nearly all the time.....
Very often.....
Sometimes.....
Not at all.....

I still enjoy the things I used to enjoy:

Definitely as much.....
Not quite so much.....
Only a little.....
Hardly at all.....

I get a sort of frightened feeling like 'butterflies' in the stomach:

Not at all.....
Occasionally.....
Quite often.....
Very often.....

I get a sort of frightened feeling as if something awful is about to happen:

Very definitely and quite badly.....
Yes, but not too badly.....
A little, but it doesn't worry me.....
Not at all.....

I have lost interest in my appearance:

Definitely.....
I don't take so much care as I should..
I may not take quite as much care.....
I take just as much care as ever.....

I can laugh and see the funny side of things:

As much as I always could.....
Not quite so much now.....
Definitely not so much now.....
Not at all.....

I feel restless as if I have to be on the move:

Very much indeed.....
Quite a lot.....
Not very much.....
Not at all.....

Worrying thoughts go through my mind:

A great deal of the time.....
A lot of the time.....
From time to time but not too often ...
Only occasionally.....

I look forward with enjoyment to things:

As much as ever I did.....
Rather less than I used to.....
Definitely less than I used to.....
Hardly at all.....

I feel cheerful:

Not at all.....
Not often.....
Sometimes.....
Most of the time.....

I get sudden feelings of panic:

Very often indeed.....
Quite often.....
Not very often.....
Not at all.....

I can sit at ease and feel relaxed:

Definitely.....
Usually.....
Not often.....
Not at all.....

I can enjoy a good book or radio or TV programme:

Often.....
Sometimes.....
Not often.....
Very seldom.....

Do not write below this line

PROGNOSIS AND TREATMENT PERCEPTIONS QUESTIONNAIRE (PTPQ)

PATIENT VERSION

1. Patients differ in the amount of information that they want to know about their *diagnosis and treatment*—some want to know everything, others want to know very little. What is your preference for details of information about your diagnosis and treatment? *Please check one.*
 - I prefer not to hear a lot of details
 - I want to hear details only in certain situations, such as when tests are abnormal or when treatment decisions need to be made
 - I want to hear as many details as possible in all situations relating to my cancer and its treatment
2. How would you rate the quality of the information you have been given by your oncologist about *treatment* and the treatment choices available for you? *Please check one.*
 - Excellent
 - Good
 - Satisfactory
 - Fair
 - Poor
3. If you had to choose one, what would you say is *your primary goal* of your current cancer treatment? Many of these goals may be important to you, but *please check the one goal* that you feel is most important to you right now.
 - To lessen my suffering as much as possible
 - For me and/or my family to be able to keep hoping
 - To make sure I have done everything
 - To extend my life as long as possible
 - To cure my cancer
 - To help cancer research
 - Other: please specify _____
4. If you had to choose one, what would you say is *your oncologist's primary goal* of your current cancer treatment? *Please check one.*
 - To lessen my suffering as much as possible
 - For me and/or my family to be able to keep hoping
 - To make sure I have done everything
 - To extend my life as long as possible
 - To cure my cancer
 - To help cancer research
 - Other: please specify _____
5. How *important* is it for you to know about **the likely outcome of your cancer over time** (i.e. your prognosis)? *Please check one.*
 - Extremely important
 - Very important
 - Somewhat important
 - A little important
 - Not at all important

6. How often have you had a conversation with your oncologist about **the likely outcome of your cancer over time** (i.e. your prognosis)? *Please check one.*

Never
 Rarely
 Sometimes
 Often
 Very Often

7. All things considered, how do you feel about the amount of information you know **about the likely outcome of your cancer over time** (i.e. your prognosis)? *Please check one.*

I wish I had more information about my prognosis
 I now have about the right amount of information
 I wish I had less information about my prognosis

8. How would you rate the quality of the information you have been given **by your oncologist about the likely outcome of your cancer over time** (i.e. your prognosis)? *Please check one.*

Excellent
 Good
 Satisfactory
 Fair
 Poor

9. Patients often report that knowing about **the likely outcome of their cancer over time** (i.e. their prognosis) impacts other decisions they have to make. Please check one box for each statement. If you do not know at all about your prognosis, please skip this question.

How helpful has knowing about your prognosis been for you in the following areas?

	Extremely Helpful	Very Helpful	A Little Helpful	Not at all Helpful
Making decisions about treatment				
Preparing for the future				
Maintaining hope				
Coping with the disease				
Overall, how helpful has knowing about prognosis been for you?				

10. How would you describe your current medical status? *Please check one.*

Relatively healthy
 Relatively healthy and terminally ill
 Seriously ill and not terminally ill
 Seriously ill and terminally ill

11. How likely do you think it is that you will be cured of cancer? *Please check one.*
 - Extremely likely (more than a 90% chance of cure)
 - Very likely (75-90% chance of cure)
 - Moderately likely (50-74% chance of cure)
 - Somewhat likely (25-49% chance of cure)
 - Unlikely (10-24% chance of cure)
 - Very unlikely (less than 10% chance of cure)
 - No chance (0% chance of cure)

12. Have you and your oncologist discussed any particular wishes you have about the care you would want to receive if you were dying? *Please check one.*
 - Yes
 - No

13. If you had to choose, would you prefer 1) a course of treatment that focused on extending life as much as possible, even if it meant more pain and discomfort, or 2) a plan of care that focused on relieving pain and discomfort as much as possible, even if that meant not living as long? *Please check one.*
 - Extend life as much as possible
 - Relieve pain as much as possible
 - Don't know

APPENDIX IV: FAMILY CAREGIVER REPORTED MEASURES

Family Caregiver Demographics Form

Please check the appropriate box or boxes.

1. Age ____

2. Gender (Mark one with an X.)

- Male
- Female

3. Relationship to patient (Mark one with an X.)

- Married or living as if married
- Living together as roommates
- Divorced/Separated
- Child (daughter or son)
- Parent (mother or father)
- Sibling (brother or sister)
- Friend
- Other (specify) _____

4. Race (Mark one with an X.)

(Choose the race which most accurately describes you.)

- American Indian or Alaskan Native
- Asian
- Black or African American
- Native Hawaiian or other Pacific Islander
- White
- Not reported
- Unknown

5. Ethnicity (Mark one with an X.)

- Hispanic or Latino
- Not Hispanic or Latino
- No reported
- Unknown

6. Religion (Mark one with an X.)

- Catholic
- Protestant
- Jewish
- Muslim
- None
- Unknown
- Not reported
- Other (specify) _____

7. What is the highest grade you finished in school? (Mark one with an X.)

- 8th grade or less
- 9th – 11th grade
- High school graduate/GED
- Associate degree/some college
- Vocational/technical school
- Bachelor's degree
- Advanced degree
- I prefer not to answer

8. What is your marital status? (Mark one with an X.)

- Married
- Domestic partnership
- Widowed
- Divorced
- Separated
- Never married
- I prefer not to answer
- Unknown/Not reported

9. With whom do you live? (Mark all that apply with an X.)

- Spouse/partner
- Girlfriend/boyfriend
- Children aged 18 years or younger
- Children aged 19 years or older
- Parent(s)/parent(s)-in-law
- Live alone
- Other (specify) _____
- Other relative (specify) _____

10. What is your current employment status? (Mark one with an X.)

(Choose the most appropriate answer.)

- Employed 32 hours or more per week
- Employed less than 32 hours per week
- Retired
- Disabled
- Full-time student
- Part-time student
- Homemaker
- On medical leave
- Only temporarily laid off, sick leave, or maternity leave
- Unemployed
- Unknown
- Other (specify) _____

11. Please indicate how long you have known the patient _____ years

12. Do you live in the same residence as the patient? (Mark one with an X.)

- Yes
- No

The SF-36v2™ Health Survey

Instructions for Completing the Questionnaire

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

EXAMPLE

This is for your review. Do not answer this question. The questionnaire begins with the section *Your Health in General* below.

For each question you will be asked to fill in a bubble in each line:

1. How strongly do you agree or disagree with each of the following statements?

	Strongly Agree	Agree	Uncertain	Disagree	Strongly disagree
a) I enjoy listening to music.	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b) I enjoy reading magazines.	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please begin answering the questions now.

Your Health in General

1. In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor	GH01
<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅	

2. Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago	HT
<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅	

Please turn the page and continue

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, Not limited at all	
a) Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF01
b) Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF02
c) Lifting or carrying groceries	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF03
d) Climbing several flights of stairs	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF04
e) Climbing one flight of stairs	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF05
f) Bending, kneeling, or stooping	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF06
g) Walking more than a mile	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF07
h) Walking several hundred yards	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF08
i) Walking one hundred yards	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF09
j) Bathing or dressing yourself	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	PF010

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	
a) Cut down on the amount of time you spent on work or other activities	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅	RP01
b) Accomplished less than you would like	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅	RP02
c) Were limited in the kind of work or other activities	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅	RP03
d) Had difficulty performing the work or other activities (for example, it took extra effort)	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅	RP04

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	
a) Cut down on the amount of time you spent on work or other activities	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	RE01
b) Accomplished less than you would like	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	RE02
c) Did work or other activities less carefully than usual	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	RE03

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely	
<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	SF01

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe	
<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6	BP01

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely	
<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	BP02

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	
a) did you feel full of life?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	VT01
b) have you been very nervous?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	MH01
c) have you felt so down in the dumps that nothing could cheer you up?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	MH02
d) have you felt calm and peaceful?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	MH03
e) did you have a lot of energy	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	VT02
f) have you felt downhearted and depressed?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	MH04
g) did you feel worn out?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	VT03
h) have you been happy?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	MH05
i) did you feel tired?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	VT04

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅

SF02

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a) I seem to get sick a little easier than other people	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅
b) I am as healthy as anybody I know	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅
c) I expect my health to get worse	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅
d) My health is excellent	<input type="radio"/> O ₁	<input type="radio"/> O ₂	<input type="radio"/> O ₃	<input type="radio"/> O ₄	<input type="radio"/> O ₅

GH02

GH03

GH04

GH05

Hospital Anxiety and Depression Scale

Name:

Date:

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he will be able to help you more.

This questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought-out response.

Tick only one box in each section

I feel tense or 'wound up':

Most of the time.....
A lot of the time.....
Time to time, Occasionally.....
Not at all.....

I feel as if I am slowed down:

Nearly all the time.....
Very often.....
Sometimes.....
Not at all.....

I still enjoy the things I used to enjoy:

Definitely as much.....
Not quite so much.....
Only a little.....
Hardly at all.....

I get a sort of frightened feeling like 'butterflies' in the stomach:

Not at all.....
Occasionally.....
Quite often.....
Very often.....

I get a sort of frightened feeling as if something awful is about to happen:

Very definitely and quite badly.....
Yes, but not too badly.....
A little, but it doesn't worry me.....
Not at all.....

I have lost interest in my appearance:

Definitely.....
I don't take so much care as I should..
I may not take quite as much care.....
I take just as much care as ever.....

I can laugh and see the funny side of things:

As much as I always could.....
Not quite so much now.....
Definitely not so much now.....
Not at all.....

I feel restless as if I have to be on the move:

Very much indeed.....
Quite a lot.....
Not very much.....
Not at all.....

Worrying thoughts go through my mind:

A great deal of the time.....
A lot of the time.....
From time to time but not too often ...
Only occasionally.....

I look forward with enjoyment to things:

As much as ever I did.....
Rather less than I used to.....
Definitely less than I used to.....
Hardly at all.....

I feel cheerful:

Not at all.....
Not often.....
Sometimes.....
Most of the time.....

I get sudden feelings of panic:

Very often indeed.....
Quite often.....
Not very often.....
Not at all.....

I can sit at ease and feel relaxed:

Definitely.....
Usually.....
Not often.....
Not at all.....

I can enjoy a good book or radio or TV programme:

Often.....
Sometimes.....
Not often.....
Very seldom.....

Do not write below this line

PROGNOSIS AND TREATMENT PERCEPTIONS QUESTIONNAIRE (PTPQ)

FAMILY CAREGIVER VERSION

1. Patients differ in the amount of information that they want to know about their *diagnosis and treatment*—some want to know everything, others want to know very little. What is your loved one's preference for details of information about their diagnosis and treatment? *Please check one.*
 - They prefer not to hear a lot of details.
 - They want to hear details only in certain situations, such as when tests are abnormal or when treatment decisions need to be made.
 - They want to hear as many details as possible in all situations relating to their cancer and its treatment.

2. How would you rate the quality of the information your loved one has been given by their oncologist about *treatment* and the treatment choices available? *Please check one.*
 - Excellent
 - Good
 - Satisfactory
 - Fair
 - Poor

3. If you had to choose one, what would you say is *your loved one's primary goal* of their current cancer treatment? Many of these goals may be important to them, but *please check the one goal* that you feel is most important to them right now.
 - To lessen their suffering as much as possible
 - For them and/or their family to be able to keep hoping
 - To make sure they have done everything
 - To extend their life as long as possible
 - To cure their cancer
 - To help cancer research
 - Other: please specify _____

4. If you had to choose one, what would you say is *your loved one's oncologist's primary goal* of their current cancer treatment? *Please check one.*
 - To lessen their suffering as much as possible
 - For them and/or their family to be able to keep hoping
 - To make sure they have done everything
 - To extend their life as long as possible
 - To cure their cancer
 - To help cancer research
 - Other: please specify _____

5. How *important* is it for your loved one to know about **the likely outcome of their cancer over time** (i.e. their prognosis)? *Please check one.*
 - Extremely important
 - Very important
 - Somewhat important
 - A little important
 - Not at all important

6. How often has your loved one had a conversation with their oncologist about **the likely outcome of their cancer over time** (i.e. their prognosis)? *Please check one.*

Never
 Rarely
 Sometimes
 Often
 Very Often

7. All things considered, how do you feel about the amount of information your loved one knows about **the likely outcome of their cancer over time** (i.e. their prognosis)? *Please check one.*

They wish they had more information about their prognosis.
 They now have about the right amount of information.
 They wish they had less information about their prognosis.

8. How would you rate the quality of the information your loved one has been given by **their oncologist about the likely outcome of their cancer over time** (i.e. their prognosis)? *Please check one.*

Excellent
 Good
 Satisfactory
 Fair
 Poor

9. Patients often report that knowing about **the likely outcome of their cancer over time** (i.e. their prognosis) impacts other decisions they have to make. Please check one box for each statement. If your loved one does not know at all about their prognosis, please skip this question.

How helpful has knowing about their prognosis been for your loved one in the following areas?

	Extremely Helpful	Very Helpful	A little Helpful	Not at all Helpful
Making decisions about treatment				
Preparing for the future				
Maintaining hope				
Coping with the disease				
Overall, how helpful has knowing about prognosis been for your loved one?				

10. How would you describe your loved one's current medical status?

Relatively healthy
 Relatively healthy and terminally ill
 Seriously ill and not terminally ill
 Seriously ill and terminally ill

11. How likely do you think it is that your loved one will be cured of cancer? *Please check one.*
 Extremely likely (more than a 90% chance of cure)
 Very likely (75-90% chance of cure)
 Moderately likely (50-74% chance of cure)
 Somewhat likely (25-49% chance of cure)
 Unlikely (10-24% chance of cure)
 Very unlikely (less than 10% chance of cure)
 No chance (0% chance of cure)

12. Has your loved one and their oncologist discussed any particular wishes about the care they would want to receive if they were dying? *Please check one.*
 Yes
 No

13. If your loved one had to choose, would they prefer 1) a course of treatment that focused on extending life as much as possible, even if it meant more pain and discomfort, or 2) a plan of care that focused on relieving pain and discomfort as much as possible, even if that meant not living as long? *Please check one.*
 Extend life as much as possible
 Relieve pain as much as possible
 Don't know

APPENDIX V: PATIENT RECRUITMENT

Suggested Language for Clinicians Offering the Study to Eligible Patients/Families

I'd like to talk to you about a different kind of study. Most studies or clinical trials focus on treatments for your x cancer. However, the goal of this study is to figure out the best way to support you and your family as you face your cancer diagnosis. Patients with x cancer often have symptoms which are difficult to manage, such as pain and fatigue, and both the patient and their family members often feel distressed or worried about their diagnosis. *The goal of this study is to figure out the best way to help patients and families with these important aspects of their care.*

The study is looking at *adding an additional team – called the palliative care team* – on top of your regular cancer care team to see if having them involved earlier is helpful for you and your family. Participating in this study will not interfere with or impact your cancer treatment in any way.

Palliative care clinicians assist patients with their symptoms and help patients and families cope with their cancer and make decisions about their care. Traditionally, these doctors and nurses only meet people when they are very ill or in the hospital. *The goal of this study is to see if having the palliative care team care for you earlier in your illness will be helpful for you and your family.*

This is a randomized study – so ½ of the people will be “coin flipped” to regular or usual care where we would only ask this team to see you if we felt like we needed their help and ½ will have this team follow you along with me and pitch in all throughout your cancer treatment.

This study is very little work for you. If you are “coin flipped” to see the palliative care team early, we will ask them to see you on the same day as me or during your chemotherapy treatments so you won’t need to make extra visits.

Whether you see the team early or not – we will ask you to complete about 30 minutes of questionnaires four times over the course of your illness; today and in 6, 12, and 24 weeks – so again, not a lot of work for you. *Remember the goal of this study is to see which care model is most helpful for patients and their families so these questions measure things like your symptoms, mood, and how you are coping so we can figure out which strategy is best.*

Important Reminders When Discussing the Study:

1. Palliative care is NOT hospice or end-of-life care. The goal of palliative care is to help patients live as well as they can for as long as they can.
2. The palliative care team will not “force” people to talk about death and dying or other topics they are not ready to discuss.
3. Patients’ cancer treatment or treatment clinical trials will NOT be impacted by their participation in this study.
4. Patients without willing family members are still able to participate.

APPENDIX VI: PC WEB-BASED TRAINING INSTRUCTIONS

Cultivating prognostic awareness: A longitudinal framework

This four-part online webinar series prepares palliative care clinicians to care for oncology outpatients.

The goal of the training courses will be to educate the clinicians on ways in which the provision of outpatient palliative care differs from inpatient delivery models. These courses will be informed by the educational needs assessment and focus on two areas: (1) Psychosocial aspects of outpatient palliative care, specifically the cultivation of prognostic awareness and the promotion of adaptive patient coping strategies over the course of the illness; and (2) developing a collaborative practice with oncology clinicians through role definition and joint patient visits.

Instructions for completing the web-based training are as follows:

1. At least one leader of the outpatient PC clinic register with the Partners Healthcare website: [REDACTED]

After following the link to the Partners Healthcare website, select 'Register'.

2. For Partners Employees, click 'Login using your Partners username'. All other first time users, click 'Create Account'.
3. Enter the required information (indicated by red asterisk) and click 'Complete Membership' at the bottom of the page.
4. Click Next at the bottom of the Activity Overview page.
5. Enter Group ID [REDACTED] and click 'Submit' (do not click on the Purchase button).
6. Select 'Physician Certificate' from the drop down box and click submit.
7. Click Next on the CME/CE Information page.
8. Click on each link and watch each training video (there are 4 parts). There will be a pretest, resource library, webinar, and posttest.
9. A certificate will be generated upon completion and you will be given the option to print it. Please print the certificate and submit to [REDACTED]
[REDACTED]

If you have any issues or questions please contact the Partners Office of Continuing Professional Development at [REDACTED].

ACCREDITATION

Partners HealthCare System is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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