# PROTOCOL TITLE:

*EL CENTRO: Engaging Latinos in the Center of Cancer Treatment Options - RCT of Usual Chemotherapy Educational Tools versus Investigational Chemotherapy Educational Tools*

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## VERSION NUMBER:

*Protocol Version #2*

## DATE:

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# 1.0 Objectives

Objective 1: Determine the impact of a multimedia chemotherapy educational intervention on understanding of chemotherapy risks and benefits among Latinos with advanced gastrointestinal cancers and their caregivers.

Objective 2: Determine the impact of the multimedia chemotherapy educational intervention on communication satisfaction and quality of informed decision-making about palliative chemotherapy among Latinos with advanced GI cancers.

Objective 3: Characterize Latino patients' & caregivers' financial well-being, financial strain, and occupational outcomes over the first 6 months of palliative chemotherapy. Explore relationships between financial strain and patients' quality of life and symptoms, and caregiver well-being.

*Hypothesis 1a:* The intervention will improve patients' understanding of the purpose and benefits of palliative chemotherapy. *(Primary outcome)*
*Hypothesis 1b:* The intervention will improve patients' understanding of the risks associated with their chemotherapy regimen. *(Secondary outcome)*
*Hypothesis 1c:* The intervention will improve caregivers' understanding of the purpose and benefits of the patients' chemotherapy.

*Hypothesis 2a:* The educational intervention will improve patients' satisfaction with communication with clinicians around treatment decision-making.
*Hypothesis 2b:* Patients who receive the intervention will be more likely to achieve their preferred role in treatment decision-making.
*Hypothesis 2c:* Patients who receive the intervention will experience less decisional conflict.

*Objective 3 is exploratory.*

# 2.0 Background*

**Patient-centered communication is an essential element of quality care for patients with advanced incurable cancer.**[1-3] Skilled and compassionate communication is a cornerstone of shared decision-making, it is necessary to equip patients with an understanding of their prognosis and treatment options, and it plays a critical role in supporting terminally-ill patients and their caregivers.[1,4] *Unfortunately the quality of patient-provider communication is suboptimal for ethnic minorities with advanced cancer,*[4-6] *particularly Latinos*.[7,8-10]

**Latinos are the largest minority group in the US, yet they suffer some of the greatest barriers to quality cancer communication.**[11] Nearly 40% of Latinos have limited English proficiency (LEP),[11] 60% have low health-literacy,[12] and Latinos have the lowest

educational attainment of any US ethnic group.[13] Use of professional interpreters partially mitigates these barriers,[14] but interpretation can also introduce errors that result in misinformation[15] and missed opportunities for rapport building.[16] It is not surprising that Latinos have high rates of dissatisfaction with their healthcare providers' communication skills.[9,10] Oncologists are similarly frustrated by their inability to communicate with Latinos effectively, and report that discussions about prognosis & treatment options are not patient-centered.[8] These co-occurring barriers uniquely compromise Latinos' ability to understand their cancer care providers and to participate optimally in their care.[10]

**Communication disparities are evidenced by gaps in Latinos' understanding about the prognosis of advanced cancer and the benefits of palliative chemotherapy.**[7,17-20] We recently reported from the Cancer Care Outcomes Research & Surveillance Consortium (CanCORS) study that an *alarming 91% of Latinos with metastatic colorectal cancer and 79% of those with metastatic lung cancer failed to understand chemotherapy was unlikely to cure their cancer*.[20] Other research demonstrates that Latino advanced cancer patients are less likely than Whites to acknowledge that they are terminally ill,[21] and have poor understanding of advance directives,[19,22] and hospice.[18] These findings belie the fact that most patients[23,24] including Latinos[25-27] want detailed information about prognosis, chemotherapy benefits, and end-of-life (EOL) care options.

**Misconceptions about prognosis and chemotherapy benefits are detrimental to the quality of advanced cancer care, and may contribute to known disparities in quality of EOL care for Latinos.** A realistic grasp of curability and prognosis is essential to patients' ability to come to terms with their illness, make value-consistent care decisions, prioritize their limited time, and plan for EOL. Patients with unrealistic expectations have been shown to prefer care focused on life-extension rather than comfort,[23,28-29] to be less likely to complete advance directives,[23] less likely to access hospice,[30] and more likely to receive intensive care near EOL.[28] These examples of poor quality EOL care[31] contribute to suffering of patients and their families,[32] and pose significant financial burdens[33] without appreciable benefit.[28,32] Because prognostic misconceptions are more common among Latinos than Whites, these knowledge gaps may partly drive Latino EOL care disparities including high rates of hospital and ICU death, underutilization of hospice, and EOL care counter to patients' preferences.[34-36] *Interventions to enhance Latino advanced cancer patients' understanding of their illness and chemotherapy options are desperately needed, and are a promising approach to reduce ethnic disparities in EOL care.*[5]

We have developed a dual Spanish/English language suite of chemotherapy educational tools with the goal of better informing patients about the risks, benefits, and goals of common chemotherapy regimens used to treat advanced GI cancers. Each chemotherapy educational tool consists of a video, website, and written booklet, and improves upon existing resources in several ways: 1) balanced discussion of benefits as well as risks, 2) focus on regimens rather than

drugs, 3) use of both written and video format, and 4) inclusion of Latino patient and provider perspectives (e.g. video clips of Latino patients describing their experiences on treatment).

The overarching objective of this project is to evaluate whether the developed chemotherapy educational toolkit improves the quality of advanced cancer care and treatment decision making by Latinos. If effective, the tools will be amenable to broad dissemination via patient accessible cancer education websites and oncology clinics.

## 3.0 Inclusion and Exclusion Criteria*

The research assistant will identify potentially eligible participants by systematically reviewing new patient and existing patient scheduling reports, as well as by accepting physician referrals. We are requesting a HIPAA waiver of authorization so that the research assistant may look in the Electronic Health Record to determine eligibility before approaching potential participants.

1) For patients presenting to oncology clinic for an initial consultation/new treatment decision regarding first-line chemotherapy for their metastatic colorectal cancer, locally advanced pancreatic cancer, or metastatic pancreatic cancer: the research assistant will identify potentially eligible patients by screening new patient scheduling reports. The research assistant will notify the oncology attending physician of the patients' potential eligibility prior to this initial consultation, will confirm the patients' potential eligibility, and will ask permission to approach the patient for participation. The study team will reach out to the clinician via email the day before a consult to ask permission to approach a potential participant. The email will contain an "opt-out" message meaning that clinicians only have to respond if they do not want a patient to be approached. Therefore, no response from a clinician will be considered as approval for a potential approach. Study research assistants will keep track of the number of potentially eligible patients, the number of physician refusals, and the reason for those refusals. Most potentially eligible patients will be approached before their initial consultation with the oncologist.
2) Oncology clinicians (physicians, nurse practitioners, physician assistants, and pharmacists from medical oncology, surgical oncology, and radiation oncology) will be able to refer eligible participants for enrollment in the study. Each site will determine the logistics of the referral process depending on its clinic model and staffing. At all sites, if the referral is made by a provider other than the attending physician, the research assistant will ask the attending physician's permission prior to approaching a patient. The research assistants will keep track of the number of potentially eligible patients referred, the number of physician refusals, and the reason for those refusals.

**Patient Inclusion Criteria:**

**Group 1 – Patients:**

- ☐ Self-identifies as Hispanic/Latino OR self-identifies with nationality from a Spanish-speaking country or territory
- ☐ Has been diagnosed with metastatic colorectal cancer (mCRC) **OR** locally advanced pancreatic cancer (LAPC) **OR** metastatic pancreatic cancer (mPC) **AND** is making a decision regarding treatment with 1st line palliative chemotherapy.
- ☐ Treating oncologist has recommended consideration of one or more of the regimens for which we have developed chemotherapy educational (CEI) toolkits
    - For mCRC: FOLFOX, FOLFOX + bevacizumab, FOLFIRI, FOLFIRI + bevacizumab
    - For LAPC or mPC: FOLFIRINOX, Gemcitabine, or Gemcitabine + nab-paclitaxel
    - Patients who are also considering treatment on a clinical trial of one of these regimens +/- an investigational agent would still be eligible, so long as the treating MD believes to the content of the CEI to be relevant to the trial regimen.
- ☐ Planning to receive treatment at the enrolling site
- ☐ Age ≥ 21
- ☐ English proficient

**Group 2 – Patients:**

- ☐ Self-identify as Hispanic/Latino OR self-identifies with nationality from a Spanish-speaking country or territory
- ☐ Has been diagnosed with metastatic colorectal cancer (mCRC) **OR** locally advanced pancreatic cancer (LAPC) **OR** metastatic pancreatic cancer (mPC) **AND** is making a decision regarding treatment with 1st line palliative chemotherapy.
- ☐ Treating oncologist has recommended consideration of one or more of the regimens for which we have developed chemotherapy educational (CEI) toolkits
    - For mCRC: FOLFOX, FOLFOX + bevacizumab, FOLFIRI, FOLFIRI + bevacizumab
    - For LAPC or mPC: FOLFIRINOX, Gemcitabine, or Gemcitabine + nab-paclitaxel
    - Patients who are also considering treatment on a clinical trial of one of these regimens +/- an investigational agent would still be eligible, so long as the treating MD believes to the content of the CEI to be relevant to the trial regimen.
- ☐ Planning to receive treatment at the enrolling site
- ☐ Age ≥ 21
- ☐ Spanish proficient

**Patient Exclusion Criteria:**

- ☐ For mCRC patients: Patients with oligometastatic disease who have a definitive plan for curative surgical resection are not eligible.
- ☐ Significant delirium/dementia as judged by the treating oncologist

**Caregiver Inclusion Criteria:**

**Group 1 – Caregivers:**

- ☐ Caregivers of eligible patient participants
- ☐ Age ≥ 21
- ☐ English proficient

**Group 2 – Caregivers:**

- ☐ Caregivers of eligible patient participants
- ☐ Age ≥ 21
- ☐ Spanish proficient

**Caregiver Exclusion Criteria:**

- ☐ Unable to comply with the study requirements per study team

This study will exclude patients who are unable to consent, individuals who are not yet adults, pregnant women, and prisoners. The study will exclude caregivers who are unable to consent, individuals who are not yet adults, and prisoners.

Also, please note: *patients will still be able to enroll in the study if they do not have a participating caregiver. Caregivers, however, can ONLY enroll with a participating patient.*

## 4.0 Study-Wide Number of Subjects*

A total of 154 subjects and up to 154 caregivers will be recruited (both English and Spanish-speaking). The study team expects to recruit 77 English-speaking patients and caregivers and 77 Spanish-speaking patients and caregivers. Assuming a subject attrition rate of 25%, which would decrease the n to 116, this sample size would give the study 80% power to detect a two-fold improvement in our primary outcome (accurate chemotherapy expectations), with a one-sided $p<0.05$. The effect size for our primary outcome is based upon conservative projections of accurate understanding regarding cure from palliative chemotherapy reported in the literature,[20,37] and based upon what would constitute a clinically meaningful improvement in understanding.

## 5.0 Study-Wide Recruitment Methods*

**Subject Recruitment:** The majority of potential subjects will be recruited at their initial consultation with the oncologist at participating study sites. Potential subjects will be approached by study research assistants prior to their consultation and offered participation in a study seeking to study a new tool to enhance education around cancer treatment options. The RA will discuss the overall aims

of the study (to improve understanding around cancer treatments), the study intervention (educational tools) and assessments (surveys). If the patient agrees to participate the RA will obtain written informed consent at that time.

If it is not possible for logistic reasons to approach the patient prior to the initial consultation, or if the patient asks the RA to come back later, potential subjects may also be recruited after their initial consultation with the oncologist, but not after they have received their first chemotherapy infusion. If the subject meets eligibility criteria but was not approached prior to their consultation, the study RA will approach the potential subject, either at the conclusion of the initial consultation, or at a subsequent visit prior to the initiation of chemotherapy. The RA will again describe the study and offer the potential subject the opportunity to participate. If the subject agrees to participate, the RA or an authorized member of the study staff will obtain written informed consent at that time.

**Identifying Potential Participants:** The research assistant will identify potentially eligible participants by reviewing patient scheduling reports, as well as by accepting physician referrals. We are requesting a HIPAA waiver of authorization so that the research assistant may look in the Electronic Health Record to determine eligibility before approaching potentially eligible participants.

1) For patients presenting to oncology clinic for an initial consultation/new treatment decision regarding first-line chemotherapy for their metastatic colorectal cancer, locally advanced pancreatic cancer, or metastatic pancreatic cancer: the research assistant will identify potentially eligible patients by screening new patient scheduling reports. The research assistant will notify the oncology attending physician of the patients' potential eligibility prior to this initial consultation, will confirm the patients' potential eligibility, and will ask permission to approach the patient for participation. The study team will reach out to the clinician via email the day before a consult to ask permission to approach a potential participant. The email will contain an "opt-out" message meaning that clinicians only have to respond if they do not want a patient to be approached. Therefore, no response from a clinician will be considered as approval for a potential approach. Study research assistants will keep track of the number of potentially eligible patients, the number of physician refusals, and the reason for those refusals. Most potentially eligible patients will be approached before their initial consultation with the oncologist.
2) Oncology clinicians (physicians, nurse practitioners, physician assistants, and pharmacists from medical oncology, surgical oncology, and radiation oncology) will be able to refer eligible participants for enrollment in the study. Each site will determine the logistics of the referral process depending on its clinic model and staffing. At all sites, if the referral is made by a provider other than the attending physician, the research assistant will ask the attending physician's permission prior to approaching a patient. The research assistants will keep track of the number of potentially eligible patients referred, the number of physician refusals, and the reason for those refusals.

All potential subjects will be approached by a study research assistant or referred by an oncology provider. Advertisements (printed, audio, or video), will not be used to recruit subjects in this study.

## 6.0 Multi-Site Research*

All sites will have the most current version of the protocol, consent document, and HIPAA authorization. All required approvals (the initial and continuing reviews, and any modifications) will be obtained at each site. This includes approval by each site's IRB of record. All modifications will be communicated to participating sites and approved by the IRBs of record before the modifications are implemented. All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies. All local site investigators will conduct the study in accordance with applicable federal regulations and local laws. All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

Prior to patient enrollment, there will be a site initiation visit webinar to orient all investigators, research assistants, and study staff to study procedures, including eligibility criteria, and procedures for subject recruitment and study assessments. Following study commencement, there will be regular check-ins with study staff led by the study project manager (PM) and/or PI by conference call. These will initially take place weekly. Once deemed appropriate by the study PI, the co-investigators, and PM, the frequency of these check-ins will decrease to monthly and will continue for the duration of the study.

Participating sites will receive regular updates during the weekly, then monthly conference calls with the project manager. For urgent updates, such as those relating to problems (inclusive of reportable events), the PI and project manager will contact site investigators and study staff by phone and email. Ad hoc conference calls will be convened as necessary. To the extent they are available, interim results will be communicated to participating sites during the regular conference calls and will be summarized via email. The closure of the study will be communicated to participating sites via an email from the study PI to the site investigators and study staff.

## 7.0 Study Timelines*

Individual subjects (patients and caregivers) will participate in the study for 6-8 months. Their participation run from the time of informed consent to the completion of the final study assessment, which takes place between 6 and 8

months after either the initiation of chemotherapy or the decision not to initiate chemotherapy.

We anticipate it will take 20 months to enroll all study subjects. Given the target sample size of 154 and that there are 6 participating sites, this timeline accounts for the enrollment of just over 1 subject and caregiver per month at each site, which we believe is reasonable and attainable given our knowledge of each site and its Latino GI cancer patient population.

We estimate that we will complete primary analyses for the study after 24 months. Assuming enrollment is complete over 20 months, all data for the primary and secondary outcomes will be obtained by 23 months (at the 3-month assessment). We estimate it will take 1 additional month to complete primary analyses. Exploratory outcomes will take an additional 5 months to collect (at the 6-8-month assessment) and analyze and will therefore be completed by 29 months after study initiation.

## 8.0 Study Endpoints*

Objective 1: Determine the impact of a multimedia chemotherapy educational intervention on understanding of chemotherapy risks and benefits among Latinos with advanced gastrointestinal cancers and their primary informal caregivers.

- Understanding of chemotherapy benefits: The primary study outcome is *the proportion of patients who have accurate understanding of chemotherapy benefits*, assessed at the 8-12-week follow-up. Patients and caregivers will be asked a single item from the CanCORS study[20]: "After talking with your doctors...how likely do you think chemotherapy is to cure your cancer?" Options: very likely, somewhat likely, a little likely, not at all likely, or don't know. Responses will be dichotomized into accurate (not at all likely) and inaccurate (all others). Our primary outcome assessment has been successfully used among thousands of patients in the CanCORS study,[20] and in a prior trial of our parent intervention, with little missing data. This outcome is relevant because it reflects core understanding required for informed consent; and it is predictive of hospice utilization.[30] The 8-12 week timepoint was chosen to allow participants adequate time to review the intervention and discuss the information with their family and care providers. The post-decision assessment will have several other secondary assessments of patients understanding of chemotherapy benefits. This will include an item assessing their understanding of the purpose of the treatment (e.g. to cure, prolong life or palliate symptoms), and how likely they believe the treatment is to shrink their cancer. At 8-12 weeks' patients and caregivers will be asked to estimate life expectancy, and will be asked about the typical prognosis of their cancer, using methods described by Weinfurt et al.[38] Prognostic understanding will be analyzed as an ordinal variable, and dichotomized into realistic or unrealistic[39] based upon published survival statistics.[40-42]
- Understanding of chemotherapy risks. At the post-decision assessment, patients will answer a series of 6 items asking how likely they believe they are to

experience specific chemotherapy side effects (fatigue, nausea/vomiting, neuropathy, myalgias/arthralgias, hair loss, diarrhea) using a 4-point likert scale (not at all likely to very likely). Patients' responses to each question will be compared to the known side effect profile of their chemotherapy regimen, and characterized as accurate or inaccurate. The responses to all 6 questions will then be summed for a composite knowledge score.

Objective 2: Determine the impact of the multimedia chemotherapy educational intervention on communication satisfaction and quality of informed decision-making about palliative chemotherapy among Latinos with advanced GI cancers.

Communication satisfaction: will be assessed by five communication satisfaction items from the validated and widely used Consumer Assessment for Health Providers and Systems (CAHPS) Cancer Survey[43]: "How often did your doctor...listen carefully to you, explain things in a way that was easy to understand, seem to know important information about your medical history, spend enough time with you, and show respect for what you had to say?" Options: always, usually, sometimes, or never.[44] Patient responses will be summed, with possible score of 0-100 (with higher scores indicating better communication) and then categorized into tertiles. Patients will complete this assessment at the post-decision and 3-month survey, but our primary analysis for this outcome will consider the post-decision assessment because it is most proximate to chemotherapy decision-making and exposure to the intervention.

- Satisfaction with the CEI tools and process: At the post-decision assessment, patients will rate their satisfaction with the CEI or standard chemotherapy education tools using a Likert scale ranging from Very Poor to Excellent. Patients in the CEI arm will provide several other assessments of the intervention, which will not be used for comparative testing.
- Decisional conflict: At the post-decision assessment, patients will assess decisional conflict using the 4 question SURE decisional conflict screening assessment developed by Legare et al.[45] A score of $\leq 3$ is indicative of decisional conflict.
- Decisional involvement: Whether patients achieved their desired degree of involvement in decision-making (patient-controlled, shared, or physician controlled) will be assessed post-decision using the modified Control Preferences Scale and compared with desired involvement (measured at baseline) using methods described elsewhere and widely used in decision aid trials.[46]
- Decisional regret: Patient decisional regret will be assessed at 8-12 weeks using 5-item Decisional Regret Scale developed by Brehaut et al.[47]
- Advance care planning: At 8-12 weeks and 6 months, patients will indicate whether they have designated a healthcare proxy, or discussed end-of-life wishes with their physicians or proxy.

**Objective 3 (Exploratory):** Characterize Latino patients' & caregivers' financial well-being, financial strain, and occupational outcomes over the first 6 months of palliative

chemotherapy. Explore relationships between financial strain and patients' quality of life and symptoms, and caregiver wellbeing.

Patients' quality of life, occupational and financial well-being will be assessed at baseline, 3 months, and 6 months to allow for evaluation of the outcomes over the first 6 months of treatment.

- Quality of life: Patient and caregiver quality of life will be assessed using the 10-item PROMIS Global Health Short Form[48], which will be administered at all survey time points.
- Symptoms: Patient symptoms will be measured using items from the PRO-CTCAE[49] that have been developed to reflect the expected and most common side effects and symptoms associated with mCRC and pancreatic cancer.
- Occupation: Patient and caregiver occupation will be assessed using questions adapted from the National Health and Nutrition Examination Survey (NHANES)[50] that assess occupational status and reasons for not working. Hours worked will also be assessed.
- Income: Total household income and the number of individuals living in the household will be assessed and benchmarked with the Federal Poverty Limit (for 1-8 household members).
- Household material hardship: Patient and caregiver household material hardship will be assessed using 3 questions from Children's Healthwatch that assess whether patients have been unable to pay their rent or mortgage, have had their electricity/gas/oil shut off for not paying bills or have experience significant food insecurity.[51-53]
- Financial toxicity: Financial toxicity will be assessed using items adapted from the literature that assess cost-shifting (e.g. taking out a new mortgage or loans) and care-altering behaviors (e.g. not filling a prescription or skipping a recommended test) due to the costs of cancer care, in addition to catastrophic financial consequences (e.g. declaring bankruptcy, having home or car repossessed).[54-56]
- Financial strain**:** Patient and caregiver financial strain will be assessed at baseline, 3 months, and 6 months using measures derived from CanCORS and from the literature. Patients and caregivers will be asked "to what degree have the costs of cancer treatment been a financial burden for you or your family?" Response options range from not a financial burden at all to a catastrophic financial burden.[57]
- Caregiver wellbeing: Caregiver quality of life, anxiety, depression, and emotional support will be assessed using PROMIS measures.[48] Caregiver support will be assessed using questions from the California Universal Caregiver Assessment.[58] Caregiver burden will be assessed using the Zarit Burden Interview.[59] Caregiver health behaviors will be assessed using items adapted from the literature that ascertain whether caregivers have delayed or otherwise altered their care due to their caregiving responsibilities.[60]

**Additional exploratory outcomes:** End-of-study chart abstraction will assess the

duration and type of chemotherapy, hospitalizations, ER visits, and survival. These chart abstractions will be performed at 6 months.

**Study Covariates** assessed at baseline will include age, sex, race/ethnicity, marital status, education, and insurance. Given our focus on Latinos we will collect information on nativity/country of origin, and acculturation (using the Marin scale[61] for language preference). Health literacy and numeracy will be assessed using measures found in the literature.[62-63] Patients will report religious affiliation & religiousness/spirituality,[64] which influence prognostic beliefs,[23] EOL care preferences,[65] and care.[66] Sources of health information will be assessed using items found in the HINTS survey.[67-68]

There are no primary or secondary safety endpoints for this project.

## 9.0 Procedures Involved*

This is a non-blinded randomized controlled trial of 154 patients with advanced colorectal or pancreatic cancer who are candidates to receive chemotherapy and their caregivers. Eligible patients will be randomized to receive either standard chemotherapy education or an enhanced chemotherapy education intervention (CEI) developed by our study team and consisting of a booklet and a video hosted on a secure website. Patients' and their caregivers' will be assessed at multiple time points throughout the study period on a variety of domains, including their understanding of chemotherapy's risks and benefits, the patient's prognosis, communication with their providers around treatment decisions, quality of life, financial well-being, and a variety of sociodemographic factors.

The study schema can be found in Figure 1 below:

**Figure 1. Study Schema**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Study Procedures & Assessments** | **Enrollment**<br>▪Screening<br>▪Eligibility<br>▪Sign consent for study | **Baseline Survey**<br>▪Demographics<br>▪Psychosocial characteristics<br>▪Clinical characteristics<br>▪Communication preferences<br>▪Quality of life/symptoms<br>▪Financial well-being | | **Post-Decision Survey**<br>▪Knowledge<br>▪Decision quality<br>▪Communication & care satisfaction<br>▪Quality of life/symptoms<br>▪MD relationship | **Follow-up Survey 1 (8-12weeks)**<br>▪Knowledge<br>▪Care satisfaction<br>▪Quality of life/symptoms<br>▪Advance care planning<br>▪Financial well-being<br>▪Caregiver burden and distress | **Follow-up Survey 2 (6-8 months)**<br>▪Quality of life<br>▪Financial well-being<br>▪Advance care planning<br>▪Caregiver burden and distress |
| **Data Sourc** | **▪Patient<br>▪Caregiver<br>▪Oncologist** | **▪Patient<br>▪Caregiver<br>▪Chart abstraction** | | **▪Patient** | **▪Patient<br>▪Caregiver** | **▪Patient<br>▪Caregiver** |
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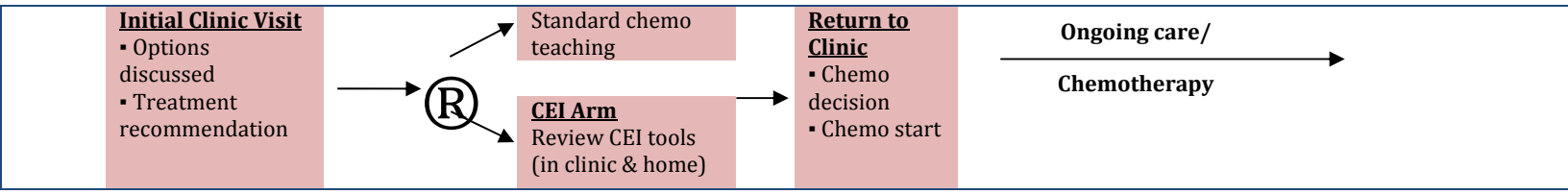


**Procedure for registration:** After the participant signs written informed consent to participate in research, the research assistant will fill out the registration form and register the participant and his/her caregiver using REDCap managed by the study team.

**Procedure for randomization (see schema above):**
After study consent and the baseline assessment, the study team will then randomize the participant to either the Usual IC Arm or the Investigational IC Arm of the study using REDCap's 1:1 randomization algorithm, stratified by whether the participant has colorectal or pancreatic cancer (diagnosis) and stratified by language preference (English or Spanish).

The name and telephone number of the research study person who will be responsible for registration and randomization is: Christine Cronin, Christine_cronin@dfci.harvard.edu, 617-632-3784.

When registering subjects, the study team will ask for the following information (see Appendices 8-9):

- Full name, telephone number, and email address of research assistant enrolling the participant
- Date subject signed informed consent
- Subject and caregiver's phone numbers, emails, and postal mail addresses (reason for collecting these: so central research assistant at Dana-Farber can administer follow-up assessments)
- Subject and caregiver's ranks of preference regarding contact method
- Subject and caregiver's gender
- Subject and caregiver's race
- Subject and caregiver's ethnicity
- Subject and caregiver's initials
- Subject and caregiver's dates of birth
- Subject ID number
- Primary oncologist
- Confirmation of eligibility
- Stratification or classification factors (colorectal or pancreatic cancer diagnosis AND English or Spanish language preference)

**Procedure for patient assessment contact and reminders:** It is acceptable to administer each assessment aloud (via phone or in-person), via email (REDCap

weblink), via iPad (REDCap), or via hard copy (in-person or postal mail). Participants and caregivers will be offered the opportunity to complete all assessments in either English or Spanish. Spanish language interpreters may assist the RA with survey administration as necessary.

The baseline assessment will be administered immediately after the participant signs informed consent, and prior to randomization. If immediate administration is not possible, the RA will follow-up with the participant up to 4 times post-informed consent. One follow-up is defined as: an in-person approach OR a phone call with an accompanying email. If the participant is non-responsive after 4 attempts, the participant will be considered to have withdrawn from the study prior to randomization.

The post-decision assessment will be administered by a research assistant at any point between the day the participant has started chemotherapy, and 3-weeks after they have received their first chemotherapy cycle. For patients who delay or decide against chemotherapy, they may complete the post-decision assessment up to 3 weeks after the decision not to pursue chemotherapy. The first follow-up assessment will be administered between 8 and 12 weeks after their first chemotherapy treatment.

The second follow-up assessment will be administered either by a central study RA at Dana-Farber or by the site research assistant, a determination that will be made by each site. The assessment will be given at any point between 6-months and 8-months post-chemo start. Prior to contacting the participant, the study staff will confirm the participant's vital status.

For all assessments, the RA can contact or approach the participant up to 4 times. One follow-up is defined as: an in-person approach OR a phone call with an accompanying email. If the participant is non-responsive after 4 attempts, then the study research assistant will mark the post-decision assessment as missing and will not contact the participant about the missing assessment.

**Procedure for caregiver recruitment:** To identify the appropriate caregiver, the RA will ask the consented patient who s/he would identify as his/her primary informal caregiver, if any. If the caregiver is physically present with the patient, the RA will provide the caregiver the study letter, explain the study, answer any questions, and ask if the caregiver would like to participate. If the caregiver verbally agrees, the RA will administer the caregiver baseline survey (available on paper, electronically, or orally per caregiver preference). If the caregiver is not physically present, the RA will send the patient home with the caregiver study letter and follow up with a phone call. When speaking to the caregiver on the phone, the RA will be sure that the caregiver has had time to read and consider the study letter. If the caregiver does not have the study letter, the RA will offer to email or postal mail a duplicate. **Because the caregiver is not always physically present at clinic visits, we are requesting waiver of documentation of consent for caregivers. This will**

**allow the RA the flexibility needed to verbally consent caregivers in person and over the phone since caregivers will not always be present in clinic.**

**Procedure for caregiver assessments and contact reminders:** It is acceptable to administer each assessment aloud (via phone or in-person), via email (REDCap weblink), via iPad (REDCap), or via hard copy (in-person or postal mail). Participants and caregivers will be offered the opportunity to complete all assessments in either English or Spanish. Spanish language interpreters may assist the RA with survey administration as necessary.

The baseline assessment will be administered immediately after the participant agrees to consent to the study, and prior to randomization. If immediate administration is not possible, the RA will follow-up with the participant up to 4 times post-informed consent. One follow-up is defined as: an in-person approach OR a phone call with an accompanying email. If the participant is non-responsive after 4 attempts, the participant will be considered to have withdrawn from the study prior to randomization.

The first follow-up assessment will be administered between 8 and 12 weeks after the patient's first chemotherapy treatment.

The second follow-up assessment will be administered either by a central study RA at Dana-Farber or by the site research assistant, a determination that will be made by each site. The assessment will be given at any point between 6-months and 8-months post-chemo start. Prior to contacting the participant, the study staff will confirm the participant's vital status.

For all assessments, the RA can contact or approach the participant up to 4 times. One follow-up is defined as: an in-person approach OR a phone call with an accompanying email. If the participant is non-responsive after 4 attempts, then the study research assistant will mark the post-decision assessment as missing and will not contact the participant about the missing assessment.

**Description of Intervention**

**Intervention Overview**: The intervention consists of 10 sets of chemotherapy educational intervention (CEI) tools. Each tool consists of a video and a complementary booklet which explain a common chemotherapy option for metastatic colorectal cancer, locally advanced pancreatic cancer, or metastatic pancreatic cancer. This suite of tools reviews the following treatment options:

- CEI Tool 1: FOLFOX & FOLFOX + bevacizumab are reviewed together in one CEI tool, comprised of a booklet and complementary video hosted on a password protected website (English Version – See Appendix 40)

- ☐ CEI Tool 2: FOLIRI & FOLFIRI + bevacizumab are reviewed together in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (English Version - See Appendix 41)
- ☐ CEI Tool 3: FOLFIRINOX is reviewed in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (English Version - See Appendix 42)
- ☐ CEI Tool 4: Gemcitabine + nab-paclitaxel is reviewed in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (English Version - See Appendix 43)
- ☐ CEI Tool 5: Gemcitabine is reviewed in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (English Version - See Appendix 44)
- ☐ CEI Tool 6: FOLFOX & FOLFOX + bevacizumab are reviewed together in one CEI tool, comprised of a booklet and complementary video hosted on a password protected website (Spanish Version – See Appendix 45)
- ☐ CEI Tool 7: FOLIRI & FOLFIRI + bevacizumab are reviewed together in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (Spanish Version – See Appendix 46)
- ☐ CEI Tool 8: FOLFIRINOX is reviewed in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (Spanish Version – See Appendix 47)
- ☐ CEI Tool 9: Gemcitabine + nab-paclitaxel is reviewed in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (Spanish Version – See Appendix 48)
- ☐ CEI Tool 10: Gemcitabine is reviewed in one CEI tool: comprised of a booklet and complementary video hosted on a password protected website (Spanish Version – See Appendix 49)

**Description of chemotherapy educational (CEI) websites:**
CEI videos and content described in the booklets will be available for patients to review at www.chemovideo.org. The website will use an individual site-specific password, with unique passwords for each of the 5 chemotherapy regimens. This will ensure that participants will only see educational information for the chemotherapy regimen(s) recommended by their doctor. Website tracking will only produce aggregate data (i.e. # of views). There will not be any website tracking that is linked to individual patient IDs.. Website content includes the main chemotherapy educational videos, two brief supplementary videos about coping, all written content from the booklets, and some supplementary content taken from well vetted online educational materials (e.g. from NCI patient educational materials).

**Description of chemotherapy educational (CEI) videos**
Each video is approximately 20 minutes and was filmed and edited by a professional health communications firm. There are both English and Spanish versions of each video. Videos and booklets are complementary but do not entirely overlap. Latino and non-Latino oncologists and nurses narrate factual information about the chemotherapy regimen of interest. "B-roll" visually illustrates potentially confusing aspects of the chemotherapy regimen (for example: a chemotherapy home infusion pump). Candid patient interviews are interspersed throughout the video to present patients' experience, with particular attention to quality of life and coping. Information about life expectancy is included as an optional link, allowing patients/caregivers a choice about whether or not to hear this information. Patients and providers in the video are diverse with respect to age, gender, and ethnicity – with a preponderance of Latinos. Videos will be accessible via a password-protected website suitable for viewing on tablet, mobile device, or computer. Website activity will be monitored. Website tracking will only produce aggregate data (i.e. # of views). There will not be any website tracking that is linked to individual patient IDs.

The structure & content of the videos are outlined below.

- *Basics*: The drugs used as part of each regimen, their route of administration, schedule, logistics of administration. A nurse demonstrates a 5FU infusion pump.
- *Risks*: Toxicities reviewed, with greatest attention to the most common toxicities, followed by rare but serious complications. Side effects specific to bevacizumab highlighted.
- *Benefits*: State that chemo alone cannot cure mCRC, locally advanced pancreatic cancer, or metastatic pancreatic cancer, and review the palliative intent of chemotherapy.
- *Alternatives*: Mention other chemotherapy regimens, clinical trials, & palliative/supportive care.

**Description of chemotherapy educational (CEI) booklets**
Booklets are regimen-specific CEI documents, which serve as a regimen-specific educational tool. There are both English and Spanish versions of each booklet with attention paid to patients' information preferences. The tools are written at an 8th grade reading level, use generic drug names, and communicate risk clearly.

- *Basics*: The drugs used as part of each regimen are outlined, along with their route of administration.
- *Benefits*: Includes the purpose of treatment (palliative, prevent symptoms, not cure).
- *Impact on prognosis*: Patients have the option of reviewing a section that describes typical life-expectancy of mCRC and pancreatic cancer with and without chemotherapy. This section is closed by a seal, and preceded by a warning to allow them to make a conscious choice of whether or not

to be exposed to this information.

- *Risks*: Most common toxicities listed in order of frequency (and approximate rates). Rare complications are listed, but de-emphasized to avoid the feel of a "laundry list."
- *Alternatives*: Clinical trials, palliative /supportive care, & other chemotherapy regimens.
- *FAQ's*: Identified by patient stakeholders
- *Question prompt list*: A list of questions developed by investigators and patient stakeholders that patients and caregivers may commonly ask their oncologists about the cancer and chemotherapy regimens.

**Randomization and Administration of Intervention**

Overview: Patients will be randomized by the study team using REDCap's 1:1 randomization algorithm. Patients randomized to the Usual CE Arm will undergo the standard institutional practice of chemotherapy education. The oncologist may also choose to give the patient the institutionally approved chemotherapy information sheets according to site-specific policies and clinical practice.

Patients randomized to the CEI Arm will be given regimen specific written and video chemotherapy educational tools developed by the study team. The treating oncologist will identify which chemotherapy regimen(s) are being considered, in order to select the appropriate chemotherapy educational tool(s) to give the patient. The patient may be given more than one CEI tool if they are considering more than one regimen. Patients randomized to the intervention arm may receive the intervention in addition to *OR* in place of the standard institutionally approved chemotherapy information sheets (both are acceptable); this is at the discretion of the treating site or the treating physician. If sites have other standard chemotherapy educational processes aside from printed teaching materials (e.g. a nurse teaching session, or a group chemotherapy class), the patient will participate in these standard teaching processes.

At the beginning of the study period, the video and booklet chemotherapy educational tools will be shared with medical oncologists, mid-level providers, or clinical staff who play a role in patient education. The purpose of this orientation is to help facilitate any subsequent conversations about the study chemotherapy educational tools that might occur between providers and patients randomized to the intervention.

**Timing of randomization and intervention delivery**: Patients will be randomized to the intervention or control arm after completing the baseline assessment and receiving a treatment recommendation from their oncologist. Randomization and delivery of the intervention will occur as soon as possible after

the initial treatment recommendation, and no later than the end of the day on their first chemotherapy treatment (see protocol schema in Figure 1).

**Administration of intervention**: After completion of the baseline assessment and randomization, a RA or the treating physician/nurse practitioner (depending site preference) will give the patient the relevant CEI booklet(s) along with printed information containing the URL address and password to the relevant CEI video(s). Patients will be encouraged to review the CEI on their own; however, the RA will also schedule a time to meet the patient to orient them to the materials and allow them to watch the video on a study iPad. This meeting will ideally be anchored to a normal chemotherapy teaching session, depending upon the participating site's usual clinical practice. If the patient does not receive the study materials at the initial consult, they will be mailed to the patient's home and the research assistant will follow-up by phone and/or email to answer any questions and schedule a time to meet in-person. Patients will be encouraged to review the CEI with their caregiver or other supporters, and to discuss any questions with their care team. The RA will be instructed not answer any clinical questions raised as a result of the CEI.

Study participants will complete 4 study assessments. Caregivers will complete 3 study assessments. Questionnaire-based instruments will be administered 1) in person by a trained research assistant at the time of a routinely scheduled visit, 2) by e-survey, 3) by phone, or 4) by postal mail. Mode of collection will be recorded. REDCap (Research Electronic Data Capture) will be used to collect and store all participant information and survey answers. REDCap is a secure, web-based, HIPAA-compliant application hosted by the Partners HealthCare Research Computing, Enterprise Research Infrastructure & iServices (ERIS) group, designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

**Each patient will be asked to complete four assessments:**

**Patient Instrument 1: Baseline Assessment (See Appendices 20,30)**
A *baseline survey* will occur immediately after enrollment and no later than the initiation of chemotherapy to assess socio-demographics, communication and information preferences, and quality of life. The baseline assessment will take approximately 15-20 minutes to complete. Patients will be compensated $10 for completing this assessment.

**Patient Instrument 2: Post-Decision Assessment (See Appendices 21,22,31, 32)**

A *post-decision survey* within 0-2 weeks of the initiation of chemotherapy will assess understanding of prognosis and chemotherapy risks/benefits; quality of informed decision-making; distress; satisfaction with the chemotherapy education process and communication. The post-decision assessment will take approximately 15-20 minutes to complete.

**Patient Instrument 3: 3-Month Follow-up Assessments (See Appendices 23,24,33,34)**
A *follow-up survey* at 8-12 weeks post-chemo start will assess stability/change in understanding of prognosis and chemotherapy benefits, patient-physician relationship, communication & care satisfaction, and financial strain. The post-decision assessment will take approximately 15-20 minutes to complete. Patients will be compensated $10 for completing this assessment.

**Patient Instrument 4: 6-Month Follow-up Assessment (See Appendices 25,35)**
A *follow-up survey* at 6-8 months post-chemo start will assess stability/change in quality of life and occupation/income, in addition to the financial strain (significant material hardship, care tradeoffs due to cost) of cancer care. Patients will be compensated $25 for completing this assessment.

**Each caregiver will be asked to complete three assessments:**

**Caregiver Instrument 1: Baseline Assessment (See Appendices 26,36)**
A *baseline survey* will occur immediately after enrollment (but *prior* to intervention exposure) to assess socio-demographics, illness understanding, communication and information preferences, and quality of life. The baseline assessment will take approximately 15-20 minutes to complete. Caregivers will be compensated $10 for completing this assessment.

**Caregiver Instrument 2: 3-Month Follow-up Assessment (See Appendices 27,37)**
A *follow-up survey* within 8-12 weeks of the patient's chemo start will assess understanding of prognosis and chemotherapy risks/benefits; quality of informed decision-making; distress; satisfaction with communication, quality of life, caregiver burden, and financial strain. The first follow-up assessment will take approximately 15-20 minutes to complete. Caregivers will be compensated $10 for completing this assessment.

**Caregiver Instrument 3: 6-Month Follow-up Assessment (See Appendices 28,29,38,39)**
A *follow-up survey* at 6-8 months post-decision will assess stability/change in quality of life and occupation/income, the financial strain (significant material hardship, care tradeoffs due to cost) of cancer care, quality of life,

and caregiver burden. The second follow-up assessment will take approximately 15-20 minutes to complete. Caregivers will be compensated $25 for completing this assessment.

**Medical Record Abstraction (see Appendices 10-11):** Research assistants will perform medical record abstraction for all enrolled patients. These medical record abstractions will be designed to assess relevant information about their clinical condition (e.g. stage at diagnosis, date of recurrence, performance status, comorbid conditions), treatment decision, and treatment experience. Information will be entered into a study specific structured medical record abstraction tool. See below for specific information to be abstracted:

- date of diagnosis; stage at diagnosis; prior adjuvant or palliative chemotherapy; date of metastatic recurrence (if relevant); comorbid medical conditions; performance status; treatment decision made (e.g., what chemotherapy regimen, clinical trial, no chemotherapy); changes in treatment (e.g. dose reductions, change in chemotherapy); results of restaging scans (disease progression, stable disease, or response); changes in treatment; medical record documentation of advance care planning; and vital status at study completion.

**NOTE:** Each site has the option to conduct the medical record review for their site's participants using the unique study ID # and enter the information into REDCap using the participants' unique study ID #. Medical records from participating sites will not be released to Dana-Farber unless the participant signs the medical record release form (Appendices 6-7).

In some cases, a participant will consent to participate in this study and begin this study while at a participating site, but then continue/transfer care at a non-participating site. In these instances, the participant will be asked to sign an optional, voluntary Global Medical Record Release Form (see Appendices 6-7) so that the central research assistant at Dana-Farber can access the participant's medical records in order to complete the study Medical Record Abstraction (Appendices 10-11).

There are 3 types of risk to this study:

- Physical risks: Physical risk to subjects in the proposed study is negligible.
- Psychological risks: Participants may experience emotional/psychological distress as a result of participating, as a result of their diagnosis of advanced GI cancer, and/or as a result of learning that palliative chemotherapy is not at all likely to cure their cancer. Participants may decide at any time and for any reason not to participate in the proposed study. The alternative to participating in the proposed study is to not participate in the proposed study in which case the patient will receive the usual care chemotherapy informed consent materials.
- Privacy risks: There is a risk of privacy violation or loss of confidentiality;

however, this is anticipated to be minimal, and the study team is committed to guaranteeing adequate protection against risk as described in the following section.

**Adequacy of Protection Against Risks**

***Recruitment and Informed Consent***

Participants will be approached by the RA in a private and confidential manner. If the patient is eligible and interested in participation, the IRB-approved IC document for research will be reviewed with and signed by the participant. The RA will keep all signed IC documents in a locked drawer, accessible only to the PI-designated study team member who holds the key.

The informed consent to participate in research documents will be approved by each site's IRB and will adhere to strict standards regarding its content. Required sections include: Introduction; Why is this research study being done? What other options are there? What is involved in the research study? How long will I be in this research study? What are the risks or discomforts of the research study? What are the benefits of the research study? Can I stop being in the research study and what are my rights? What are the costs? What happens if I am injured or sick because I took part in this research study? What about confidentiality? Whom do I contact if I have questions about the research study?

***Protection against the 3 types of risk to this study:***

- Protection against physical risks: physical risk to subjects in the proposed study is negligible.
- Protection against psychological risks: First, we are minimizing risk by our extensive process of stakeholder involvement, piloting of the CEI tools on patients/caregivers of patients with advanced GI cancer, with iterative rounds of revisions to ensure that the CEI tools developed meet the information needs and preferences of Latino cancer patients/caregivers. Any patients who exhibit psychological distress stress as result of the study tools will be referred to the patients' oncologist and social worker, or a mental health professional as appropriate.
- Protection against privacy risks: To protect PHI, the following measures will be taken. Patients will be approached and interviewed in private settings. All study form hard copies will use only de-identified unique study ID numbers and be kept in the patients' study files in locked drawers to which only the designated study team member has a key. All electronic data will be kept on Dana-Farber's secure, password protected servers as managed by the Dana-Farber Department of Research Computing and IS.

Departmental and institute-wide policies enforce the protection of our electronic information, especially with regards to HIPAA regulations and the integrity of patient care. These policies also safeguard again theft, abuse, misuse, and any form of damage. The scope of protection includes information which is printed from or stored on a

database, mainframe, server desktop, laptop, PDA, CD-ROM, hard disk, flash drive, optical platter, tape, smart phone, network, telephone, and other computer-enabled medical devices. These policies regulate usage of system IDs, passwords, e-mail accounts, anti-virus mechanisms, encryption, mobile devices, remote access, remote control software, and wireless devices. IS responsibilities and governance include firewall protection of all Dana-Farber internal networks and the internet, system evaluation, risk analysis, information access, regular review of user accounts, systems audit, regular review of remote access, and physical location access. Specific to this project, no data will be stored on laptops at any point and secure transfer protocols will be used for any electronic exchange of information. All staff/users receive mandatory institutional trainings on Information Security and must adhere to policies at all times.

Data will be collected using survey materials developed by the study team. These are attached in the appendices. Information from the medical record will be obtained through chart abstraction. The chart abstraction form is attached (Appendices 10-11).

No specimens will be collected from study participants. Data will be collected (using unique study ID numbers) from each participant on the 4 study assessments, completed in either English or Spanish. Data will also be collected from each participant's medical record via chart abstraction performed by the research staff at each site. Data will be collected (using unique study ID numbers) from each caregiver on the 3 study assessments, completed in either English or Spanish.

Summary of measures used at each patient assessment

| **Table 1: Key study outcomes, measures, and time points of assessment** | | | | | |
|---|---|---|---|---|---|
| **Domain** | **Measures** | **Baseline Assessment** | **Post-decision Assessment** | **Follow-up Assessment 1 (3 months)** | **Follow-up Assessment 2 (6 months)** |
| **Covariates** | | | | | |
| Socio-demographics | Standard assessments | • | | | |
| Health Literacy/numeracy | Self-reported health literacy/numeracy | • | | | |
| Sources of health information | Adapted from HINTS | • | • | | |
| Communication & decision-making preferences | Control Preferences Scale[46] | • | • | | |
| | Prognostic information preferences[25] | | • | | |
| Religion/spirituality | Balboni RSCC | • | | | |
| Acculturation | SASH Language subscale | | | | |
| Language concordance | Adapted from literature | • | | | |
| Use of interpreters | From CAHPS | | | • | |
| **Key Outcomes** | | | | | |
| **Aim 1: Core Understanding** | | | | | |
| Chemotherapy benefits | Adapted from CANCORS (**primary outcome**)[20] | | • | • | |

| | | | | | |
|---|---|---|---|---|---|
| Information important to treatment decision-making | Adapted from parent study | • | • | | |
| Risks, Benefits, Alternatives | Adapted from parent study[69] | | • | • | |
| Prognosis | Adapted from Coping with Cancer | | | • | |
| **AIM 2: Satisfaction with communication and care** | | | | | |
| With MD communication | 5 items from CAHPS[43,70] | | • | • | |
| With CE process/CE tools | Developed from parent study | | • | | |
| With communication around chemotherapy | PACE scale | | | • | |
| **Aim 2: Decision Making about cancer treatment** | | | | | |
| Decisional conflict | SURE | | • | | |
| Decisional involvement | Modified Control Preferences Scale[46] | • | • | | |
| Decisional regret | Decisional Regret Scale | | | • | |
| Advance care planning | Standard metrics[3] | | | • | • |
| **Aim 3: Impact of cancer on quality of life, occupation, and financial strain** | | | | | |
| Quality of life | PROMIS Global Health Short Form | • | • | • | • |
| Symptoms related to chemotherapy and GI cancer | PRO-CTCAE | • | • | • | |
| Occupation/income | Standard assessments | • | | • | • |
| Health Insurance | Standard assessments | • | | | • |
| Financial stress/strain | From CanCORS, Zafar | • | | • | • |
| Significant material hardship | From Children's Healthwatch | • | | | • |
| Adverse financial effects | Adapted from literature | | | • | • |
| Cost-shifting behaviors | Adapted from literature | | | • | • |

Summary of measures used at each caregiver assessment. All caregiver outcomes are exploratory.

**Table 2: Key study outcomes, measures, and time points of assessment**

| Domain | Measures | Baseline Assessment | Follow-up Assessment 1 (3 months) | Follow-up Assessment 2 (6-8 months) |
|---|---|---|---|---|
| **Covariates** | | | | |
| Socio-demographics | Standard assessments | • | | |
| Health Literacy/numeracy | Self-reported health literacy/numeracy | • | | |
| Religion/spirituality | Balboni RSCC | • | | |
| Acculturation | SASH Language subscale | • | | |
| **Key Outcomes** | | | | |
| **Core Understanding** | | | | |
| Chemotherapy benefits | Adapted from CANCORS [1] | | • | |

| | | | | |
|---|---|---|---|---|
| Information important to treatment decision-making | Adapted from parent study | • | | |
| Prognosis | Adapted from Coping with Cancer | | • | |
| **Satisfaction with communication and care** | | | | |
| With MD communication | 5 items from Cancer CAHPS[1] | | • | |
| **Decision Making about cancer treatment** | | | | |
| Information sharing preferences | Adapted from literature | | • | |
| Advance care planning | Standard metrics[23] | | • | |
| **Quality of life & distress** | | | | |
| Quality of life | PROMIS Global Health Short Form | • | • | • |
| Anxiety | PROMIS Anxiety Short Form | • | • | • |
| Depression | PROMIS Depression Short Form | • | • | • |
| Emotional support | PROMIS Emotional Support Short Form | • | • | • |
| Caregiver support | California Universal Caregiver Assessment | • | | • |
| Caregiver health behaviors | Adapted from literature | • | | • |
| Caregiver burden | Zarit Burden Interview | • | • | • |
| **Occupation/income/financial strain** | | | | |
| Occupation/income | Standard assessments | • | • | • |
| Health Insurance | Standard assessments | • | | |
| Financial stress/strain | From CanCORS, Zafar | | • | • |
| Significant material hardship | From Children's Healthwatch | • | | • |
| Adverse financial effects | Adapted from literature | | • | • |
| Cost-shifting behaviors | Adapted from literature | | | • |

These data will be collected at each site by a member of the study team as designated by the site's lead study investigator as overseen by the site's IRB. All original study form hard copies/source documentation will be kept in the patients' study files in locked drawers to which only the designated study team member has a key. All electronic data will be securely transmitted to the lead site (Dana-Farber Cancer Institute) via encrypted file transfer where it will be kept on Dana-Farber's secure, password-protected servers as managed by the Dana-Farber Department of Research Computing and IS. Only the DF/HCC PI and her designees as overseen by the DF/HCC IRB will have access to the data collected during this study. All data collected during this study will be collected and stored using unique study ID numbers. All data analysis will be done in-house at Dana-Farber/UMB; no data will be released to an outside institution. Stakeholders will have access to aggregate interim results, but not to individual participant or raw study data.

## 10.0 Data and Specimen Banking*

For this study, no specimens will be collected from participants. All participants will however, complete up to 4 study surveys. All original study forms (including study surveys, consent forms, registrations forms, etc.) including hard copies/source documentation will be kept in the patients' study files in locked drawers in Dana 1011 to which only the designated study team member has a key. All electronic data will be securely transmitted to the lead site (Dana-Farber Cancer Institute) via encrypted file transfer where it will be kept on Dana-Farber's secure, password-protected servers as managed by the Dana-Farber Department of Research Computing and IS. Only the DF/HCC PI and her designees as overseen by the DF/HCC IRB will have access to the data collected during this study. All data collected during this study will be collected and stored using unique study ID numbers. Data will be stored on DFCI servers for 2 years after the completion of the study.

Only the DFCI/HCC PI and her designees will have access to the data. Interim data will be released to stakeholders only in aggregate.

Study results will be available on clinicaltrials.gov and study participants will also be asked if they would like to receive overall study results during the informed consent process.

Collected study data may be stored and used for future research. If so, any personal identifiers will be removed so that the information or samples cannot be linked back to individual participants.

Investigators, including investigators from collaborating institutions, can request this data for new research. Data may also be shared with outside non-profit academic investigators as well as with for-profit pharmaceutical investigators or commercial entities, with whom we collaborate. All requests for data usage will be up to the discretion of the study PI.

## 11.0 Data Management* and Confidentiality

Primary analyses of the intervention effect will reflect the "intention to treat" principle, however, results will also be described according to participants' actual use of the intervention. Differences between study arms in our *primary outcome* (patients' understanding of chemotherapy benefits at 8-12 weeks) will be examined using the Fisher's exact test. Differences in all other patient and caregiver outcomes will be tested using Fisher's exact test (for nominal categorical outcomes), and Wilcoxon tests for ordinal measures. Subgroup analyses will explore the effect of the intervention by cancer diagnosis (colorectal or pancreatic), primary language, health literacy, and by components of the intervention utilized. Because the intervention effect may be moderated by patient characteristics (e.g., English

proficiency, degree of acculturation), interaction tests will examine treatment heterogeneity.

Descriptive statistics will explore patient/caregiver financial and occupational outcomes and financial toxicity over time. Of note, we do not expect these "outcomes" to be impacted by the intervention, but we plan to analyze them across the overall study cohort. Trajectories in these outcomes over time will be examined using paired Wilcoxon tests, or difference scores. We will also explore relationships between financial toxicity, strain and household material hardship (independent variables) and patients' and caregivers' quality of life and emotional well-being (dependent variables) using multivariable linear regressions controlling for potentially confounding sociodemographic factors. Generalized estimating equations will also examine the influence of these independent variables on relevant outcome trajectories over time.

Primary analysis for our primary and key secondary outcomes will employ multiple imputation to mitigate potential bias associated with missing data. Multiple imputation will be performed according to a "missing at random" assumption, which postulates that the missingness of data is not completely random, but may be partly accounted for by observed data.[71]

Accurate chemotherapy understanding (primary outcome): Assuming an attrition rate of 25% and a resultant n=116, this study has 88% power to detect a two-fold improvement in our primary outcome, with a one-sided $p<0.05$ (see table 3). The effect size for our primary outcome is based upon conservative projections of accurate expectations regarding cure from palliative chemotherapy reported in the literature,[20,37] and based upon what would constitute a clinically meaningful improvement in understanding.

Excellent communication rating: The study also has 88% power to detect a 50% increase in the proportion of patients providing excellent communication ratings, a clinically meaningful effect size derived from CanCORS[20], with a one-sided $p<0.05$.

Decisional conflict: In the parent study, 25% of patients in the usual care arm experienced any degree of decisional conflict. With 80% power, we will be able to detect a 17% decrease in decisional conflict with a one-sided $p<0.05$.

Achievement of desired decisional control: In the parent study, 38% of patients in the usual care arm achieved their desired level of decisional control, which is consistent with the literature.[72] With 80% power, we will be able to detect a 23% increase in achievement of desired decisional control with a one-sided $p<0.05$.

Given that multiple imputation will be used for missing data, Table 3 also presents power calculations for the recruitment goal, n=154.

Table 3: Power for primary and secondary outcome with n=116 and n=154, one-sided p<0.05

| Outcomes & source of estimate | Estimated Effect | | Power for n=116, p<0.05, one-sided | Power for n=154, p<0.05, one-sided |
|---|---|---|---|---|
| | Usual care arm | CEI arm | | |
| **Accurate chemotherapy expectations**[1,73,74] | 25% | 50% | 88% | 95% |
| **Excellent communication rating**[1] | 50% | 75% | 88% | 95% |
| **Decisional conflict** | 25% | 8% | 80% | 100% |
| **Achievement of desired decisional control** | 38% | 61% | 80% | 89% |

In order to secure all data collected during this study, the research team will work on conjunction with all departmental and institute-wide policies. These policies enforce the protection of our electronic information, especially with regards to HIPAA regulations and the integrity of patient care. These policies also safeguard against theft, abuse, misuse, and any form of damage. The scope of protection includes information which is printed from or stored on a database, mainframe, server desktop, laptop, PDA, CD-ROM, hard disk, flash drive, optical platter, tape, smart phone, network, telephone, and other computer-enabled medical devices. These policies regulate usage of system IDs, passwords, e-mail accounts, anti-virus mechanisms, encryption, mobile devices, remote access, remote control software, and wireless devices. IS responsibilities and governance including firewall protection of all Dana-Farber internal networks and the internet, system evaluation, risk analysis, information access, regular review of user accounts, systems audit, regular review of remote access, and physical location access. Specific to this project, no data will be stored on laptops at any point and secure transfer protocols will be used for any electronic exchange of information. All staff/users receive mandatory institutional trainings on Information Security and must adhere to policies at all times. All study files will be stored in a shared folder in a HIPAA-compliant Dropbox Business folder shared ONLY with the study team (all of whom have Partners Dropbox Business).

All consented patients and interested caregivers will be inputted into the Clinical Trials Management System (CTMS) OnCore as required by DF/HCC SOP REGIST-101. All Dana-Farber Participants will be registered with OnCore as soon as possible after the consenting/registration period, and always within the same day of enrollment. All external site participants will have registered with OnCore as soon as the external team notifies DFCI about the new enrollment and sends a copy of the consent form and registration form.

Appendix 5 provides the Data and Safety Monitoring Plan (DSMP) for this study. The DSMP will ensure that our DF/HCC multi-site project will comply with Federal

Regulations, Health Insurance Portability and Accountability Act (HIPAA) requirements, and applicable DF/HCC, DFCCC, and Standard Operating Procedures, and NCI Guidelines.

## 12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

This is a social behavioral research project, not a treatment protocol. The study involves questionnaire-based assessments. As such, the only adverse event that will be monitored and reported is psychological distress as determined by the treating oncologist. For any patient who exhibits severe distress as result of the study procedures, the study research assistant will notify the patients' oncologist and social worker for appropriate response, including possible mental health referral if necessary. Furthermore, participants will be reminded that participation is voluntary and can be stopped at any time for any reason.

## 13.0 Withdrawal of Subjects*

Subjects who do not complete the baseline assessment prior to the initiation of chemotherapy, or within 2 weeks of the decision not to undergo chemotherapy will be withdrawn from the research study without their consent. These patients will be informed of their withdrawal from the study by study staff.

The overall DF/HCC study PI, Dr. Andrea Enzinger, will make all decisions regarding early termination of the study. The study team will then notify all participants accordingly.

When subjects withdraw from the research, they will no longer be contacted by study staff to complete remaining assessments. Their assessments up to their withdrawal will be included in intention-to-treat analyses of the primary and secondary outcomes. If a participant withdraws consent at any time, all of their assessments will be discarded and will not be included in study analyses, unless otherwise noted by the withdrawing participant.

## 14.0 Risks to Subjects*

- Physical risks: Physical risk to subjects in the proposed study is negligible.
- Psychological risks: Participants may experience emotional/psychological distress as a result of participating, as a result of their diagnosis of advanced GI cancer, and/or as a result of learning that palliative chemotherapy is not at all likely to cure their cancer. Participants may decide at any time and for any reason not to participate in the proposed study. The alternative to participating in the proposed study is to not participate in the proposed study in which case the patient will receive the usual care chemotherapy informed consent materials.
- Privacy risks: There is a risk of privacy violation or loss of confidentiality; however, this is anticipated to be minimal, and the study team is committed to guaranteeing adequate protection against risk as described in the following

section.

**Protection Against Risks**

***Recruitment and Informed Consent***

Participants will be approached in by the RA in a private and confidential manner. If the patient is eligible and interested in participation, the IRB-approved IC document for research will be reviewed with and signed by the participant. The RA will keep all signed IC documents in a locked drawer, accessible only to the PI-designated study team member who holds the key.

The informed consent to participate in research documents will be approved by each site's IRB and will adhere to strict standards regarding its content. Required sections include: Introduction; Why is this research study being done? What other options are there? What is involved in the research study? How long will I be in this research study? What are the risks or discomforts of the research study? What are the benefits of the research study? Can I stop being in the research study and what are my rights? What are the costs? What happens if I am injured or sick because I took part in this research study? What about confidentiality? Whom do I contact if I have questions about the research study?

***Protection against the 3 types of risk to this study:***

- Protection against physical risks: physical risk to subjects in the proposed study is negligible.
- Protection against psychological risks: First, we are minimizing risk by our extensive process of stakeholder involvement, piloting of the CEI tools on patients/caregivers of patients with advanced GI cancer, with iterative rounds of revisions to ensure that the CEI tools developed meet the information needs and preferences of Latino cancer patients/caregivers. Any patients who exhibit psychological distress as a result of the study tools will be referred to the patients' oncologist and social worker, or a mental health professional as appropriate.
- Protection against privacy risks: To protect PHI, the following measures will be taken. Patients will be approached and interviewed in private settings. All study form hard copies will use only de-identified unique study ID numbers and be kept in the patients' study files in locked drawers to which only the designated study team member has a key. All electronic data will be kept on Dana-Farber's secure, password protected servers as managed by the Dana-Farber Department of Research Computing and IS.

## 15.0 Potential Benefits to Subjects*

By taking part in the research, individual subjects, particularly those randomized to the intervention, may gain an improved knowledge of the risks and benefits of the chemotherapy regimen for their cancer. This knowledge may prepare them for what lies ahead in their treatment course and may therefore improve quality of life and decrease distress. Subjects may also gain a more accurate understanding of

their prognosis, which may help facilitate end-of-life planning and the pursuit of goal-concordant care. It is our hope that the knowledge gained through this study will be durable and subjects will retain it beyond the completion of the study.

## 16.0 Vulnerable Populations*

Not applicable to this study.

## 17.0 Community-Based Participatory Research*.

Not applicable to this study.

## 18.0 Sharing of Results with Subjects*

Study results will be shared with participants in aggregate at the conclusion of primary and secondary analyses.

## 19.0 Setting

Study Setting: The study will be conducted at the Dana-Farber Cancer Institute Longwood Campus. Participants will be identified through 2 different methods: 1) direct referral from clinicians in the Gastrointestinal Oncology group and 2) review of new and existing patient scheduling reports in EPIC. For consenting purposes, both patients and caregivers will be approached in clinic in-person by a member of the research team. All study assessments can be completed in-person, over the phone, or via email in order to minimize burden on participants. This study will also be open at 6 additional academic and community oncology practices across the US, serving large and diverse Latino populations. Diversity of sites will ensure generalizability of our findings.

## 20.0 Resources Available

This study team will be taking place under the Population Sciences Division at Dana-Farber. The Population Sciences Division maintains its own server infrastructure and systems administration staff that provide data storage, data backup, and data security in support of large data analysis projects. The servers are configured as a virtual server pool with virtual server hosts connected to a centralized Storage Area Network (SAN) device. Server virtualization increases the efficiency and flexibility of the server pool while minimizing downtime and cost. The server pool currently has 20 processor cores and a data storage capacity of 9 terabytes. This server infrastructure has a dedicated Systems Administrator to optimize performance, maintain security patches, perform backups, and execute other related tasks. Researchers in the Division have access to additional resources through the Research Computing group. Research Computing provides a variety of services including file server space, backup services, website hosting, and support of some workstation computers.
Additionally, the research staff is well-qualified to perform their duties. Drs. Enzinger and Schrag have extensive experience in conducting multi-center research studies in cancer disparities, health services, and education. They have deep knowledge of the clinical and research environments and the patient population and

culture at DFCI. Dr. Lindsay has extensive experience in health disparities and socio-behavioral intervention, particularly with regard to Latino health. The project manager, Christine Cronin has significant experience in running large, multi-center trials in this area, and she has overseen the management of DF/HCC Protocol #15-143 (the parent study for this project that was funded by PCORI).

We believe that it is feasible to recruit the required number of suitable subjects within the agreed recruitment period. The GI oncology clinic at DFCI sees an average of 25-30 patients with advanced colorectal and pancreatic cancers about to start chemotherapy per month. Of these, roughly 10% are Latino. This study will also be open at 6 additional academic and community oncology practices across the US, serving large and diverse Latino populations.

Dr. Enzinger will devote 5% of her time to conducting and completing the research project. Her main responsibilities will include overseeing subject recruitment and ensuring interim project analyses. Christine Cronin, the PM will also devote 75% of her time to the oversight and management of this project.

The Population Sciences Division maintains its own server infrastructure and systems administration staff that provide data storage, data backup, and data security in support of large data analysis projects. The servers are configured as a virtual server pool with virtual server hosts connected to a centralized Storage Area Network (SAN) device. Server virtualization increases the efficiency and flexibility of the server pool while minimizing downtime and cost. The server pool currently has 20 processor cores and a data storage capacity of 9 terabytes. This server infrastructure has a dedicated Systems Administrator to optimize performance, maintain security patches, perform backups, and execute other related tasks. Researchers in the Division have access to additional resources through the Research Computing group. Research Computing provides a variety of services including file server space, backup services, website hosting, and support of some workstation computers.

Any patients who exhibit psychological distress as a result of the study tools will be referred to the patients' oncologist and social worker, or a mental health professional as appropriate. Given the nature of the intervention, there are no anticipated medical consequences of this study.

All investigators, research assistants, and study staff will be oriented to the protocol during a study-initiation webinar. During this webinar, the PI and PM will provide a detailed orientation to all study procedures and all study staff members' duties and functions. Each site will also have electronic and hard copies of the protocol which will be made available to study staff. Regular check-in conference calls with study staff will be used to provide updates on the protocol if changes have been made, discuss issues at the individual sites with regard to recruitment, administration of the intervention, assessment, or any other issue that may arise.

## 21.0 Prior Approvals

Not applicable for this study.

## 22.0 Recruitment Methods

The majority of potential subjects will be recruited at their initial consultation with the oncologist at participating study sites. These patients will be aware that they have been diagnosed with either colorectal or pancreatic cancer but will have not yet started treatment with chemotherapy. Potential subjects will be approached by study research assistants prior to their consultation and offered participation in a study seeking to study a new tool to enhance education around treatments for colorectal and pancreatic cancers. The RA will discuss the overall aims of the study (to improve education around cancer treatments), the study intervention (educational tools) and assessments (surveys). The RA will refer to cancer treatments and not mention chemotherapy specifically as these patients have not yet discussed treatment options and the potential for chemotherapy with their oncologists. If the patient agrees to participate the RA will obtain written informed consent at that time.

Potential subjects may also be recruited after their initial consultation with the oncologist. If the subject meets eligibility criteria but was not approached prior to their consultation, the study RA will approach the potential subject, either at the conclusion of the initial consultation, or at a subsequent visit prior to the initiation of chemotherapy. The RA will again describe the study and offer the potential subject the opportunity to participate. If the subject agrees to participate, the RA will obtain written informed consent at that time.

The source of subjects at DFCI will be the GI Oncology clinic where patients with colorectal and pancreatic cancers.

The research assistant will identify potentially eligible participants by systematically reviewing new patient and existing patient scheduling reports, as well as by accepting physician referrals. We are requesting a HIPAA waiver of authorization so that the research assistant may look in the Electronic Health Record to determine eligibility before approaching potential participants.

1) For patients presenting to oncology clinic for an initial consultation/new treatment decision regarding first-line chemotherapy for their metastatic colorectal cancer, locally advanced pancreatic cancer, or metastatic pancreatic cancer: the research assistant will identify potentially eligible patients by screening new patient scheduling reports. The research assistant will notify the oncology attending physician of the patients' potential eligibility prior to this initial consultation, will confirm the patients' potential eligibility, and will ask permission to approach the patient for participation. Study research assistants will keep track of the number of potentially eligible patients, the number of physician refusals, and the reason

for those refusals. Most potentially eligible patients will be approached before their initial consultation with the oncologist.

2) Oncology clinicians (physicians, nurse practitioners, physician assistants, and pharmacists from medical oncology, surgical oncology, and radiation oncology) will be able to refer eligible participants for enrollment in the study. Each site will determine the logistics of the referral process depending on its clinic model and staffing. At all sites, if the referral is made by a provider other than the attending physician, the research assistant will ask the attending physician's permission prior to approaching a patient. The research assistants will keep track of the number of potentially eligible patients referred, the number of physician refusals, and the reason for those refusals.

All potential subjects will be approached by a study research assistant or referred by an oncology provider. Advertisements (printed, audio, or video), will not be used to recruit subjects in this study.

Subjects will be paid $10 for completion of the baseline assessment. They will be paid $10 for the 8-12-week follow-up questionnaire. Participants will receive $25 for the final follow-up questionnaire given at 6-8 months.

## 23.0 Local Number of Subjects:

The study team is looking to enroll 100 total subjects and caregivers locally.

## 24.0 Provisions to Protect the Privacy Interests of Subjects

To protect PHI, the following measures will be taken. Patients will be approached and interviewed in private settings. All study form hard copies will use only de-identified unique study ID numbers and be kept in the patients' study files in locked drawers to which only the designated study team member has a key. All electronic data will be kept on Dana-Farber's secure, password protected servers as managed by the Dana-Farber Department of Research Computing and IS.

Departmental and institute-wide policies enforce the protection of our electronic information, especially with regards to HIPAA regulations and the integrity of patient care. These policies also safeguard again theft, abuse, misuse, and any form of damage. The scope of protection includes information which is printed from or stored on a database, mainframe, server desktop, laptop, PDA, CD-ROM, hard disk, flash drive, optical platter, tape, smart phone, network, telephone, and other computer-enabled medical devices. These policies regulate usage of system IDs, passwords, e-mail accounts, anti-virus mechanisms, encryption, mobile devices, remote access, remote control software, and wireless devices. IS responsibilities and governance including firewall protection of all Dana-Farber internal networks and the internet, system

evaluation, risk analysis, information access, regular review of user accounts, systems audit, regular review of remote access, and physical location access. Specific to this project, no data will be stored on laptops at any point and secure transfer protocols will be used for any electronic exchange of information. All staff/users receive mandatory institutional trainings on Information Security and must adhere to policies at all times.

Subjects will be approached for potential participation in private They will also complete all study assessments in private. At each assessment, subjects will be reminded that they can skip any questions they do not wish to answer and are free to withdraw from the study at any time.

Study research assistants will have access to subject's medical records to abstract information as discussed in other sections of this protocol. RAs will only access information that is necessary to collect for the study protocol and will not be permitted to access the medical record for other purposes.

## 25.0 Compensation for Research-Related Injury

Not applicable for this study.

## 26.0 Economic Burden to Subjects

Subjects will complete study assessments at previously scheduled oncology visits. We do not anticipate that the study will lead to any new costs for subjects.

## 27.0 Consent Process

We will be obtaining informed consent for this study. The study RAs will obtain written informed consent from subjects after they agree to participate in the study. For most subjects, this will occur immediately before their initial oncology consultation. We will follow SOP: Informed Consent Process for subjects enrolled at DFCI. Each site will follow its own institutionally-mandated informed consent procedures.

Because the caregiver is not always physically present at clinic visits, we are requesting waiver of documentation of consent for caregivers. This will allow the RA the flexibility needed to verbally consent caregivers in person and over the phone since caregivers will not always be present in clinic.

***Non-English Speaking Subjects:*** Many study participants will speak Spanish. All study materials, including informed consent forms, will be translated into Spanish by native Spanish speakers with expertise in medical oncology or health communication. Spanish speaking subjects will be approached either by Spanish-speaking research assistants, or by research assistants with professional Spanish interpreters.

## 28.0 Process to Document Consent in Writing

For patient subjects, we will follow SOP: Informed Consent Process (CON-100). For caregivers, we will be requesting a waiver of documentation of consent as they may not always be present with the patients for whom they care. All caregivers, however, will be given a study letter that contains the elements of informed consent and informs them about their involvement with this project.

See Appendices 1-2 for the model informed consent forms in Spanish and English for patient subjects. See Appendices 3-4 for consent scripts in English and Spanish for caregiver subjects.

## 29.0 Drugs or Devices

Not applicable for this study.

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## 31.0 Appendices

1. Model Informed Consent Form for External Sites (ENGLISH VERSION)
2. Model Informed Consent Form for External Sites (SPANISH VERSION)
3. Caregiver Informed Consent Study Letter (ENGLISH VERSION)
4. Caregiver Informed Consent Study Letter (SPANISH VERSION)
5. Multi-Center Data Safety Monitoring Plan
6. Global Medical Release Form (ENGLISH VERSION)
7. Global Medical Release Form (SPANISH VERSION)
8. Participant Registration Form
9. Caregiver Registration Form
10. Medical Record Abstraction Form – Pancreatic Cancer
11. Medical Record Abstraction Form – Colorectal Cancer
12. Phone script for approaching potential participants via phone (ENGLISH VERSION)
13. Phone script for approaching potential participants via phone (SPANISH VERSION)
14. Phone script for approaching potential caregivers via phone (ENGLISH VERSION)
15. Phone script for approaching potential caregivers via phone (SPANISH VERSION)
16. Phone script for assessment administration (ENGLISH VERSION)
17. Phone script for assessment administration (SPANISH VERSION)
18. Site Recruitment Checklist (ENGLISH VERSION)
19. Site Recruitment Checklist (SPANISH VERSION)

**Study Assessments**

20. Patient Baseline Assessment (ENGLISH VERSION)
    - 20a. Patient Baseline Assessment - for administration online
    - 20b. Patient Baseline Assessment - for written administration
21. Patient Post-Decision Assessment Version 1 - Usual CEI Arm (ENGLISH VERSION)
    - 21a. Patient Post-Decision Version 1 – for administration online
    - 21b. Patient Post-Decision Version 1 – for written administration
22. Patient Post-Decision Assessment Version 2 - Investigational CEI Arm (ENGLISH VERSION)
    - 22a. Patient Post-Decision Version 2 – for administration online
    - 22b. Patient Post-Decision Version 2 – for written administration
23. Patient 3-Month Follow-Up Assessment Version 1 - Usual CEI Arm (ENGLISH VERSION)
    - 23a. Patient 3-Month Follow-Up Version 1 – for administration online
    - 23b. Patient 3-Month Follow-Up Version 1 – for written administration
24. Patient 3-Month Follow-Up Assessment Version 2 - Investigational CEI Arm (ENGLISH VERSION)

- 24a. Patient 3-Month Follow-Up Version 2 – for administration online
- 24b. Patient 3-Month Follow-Up Version 2 – for written administration

25. Patient 6-Month Follow-Up Assessment (ENGLISH VERSION)
    - 25a. Patient 6-Month Follow-Up – for administration online
    - 25b. Patient 6-Month Follow-Up – for written administration
26. Caregiver Baseline Assessment (ENGLISH VERSION)
    - 26a. Caregiver Baseline Assessment – for administration online
    - 26b. Caregiver Baseline Assessment – for written administration
27. Caregiver 3-Month Follow-Up Assessment (ENGLISH VERSION)
    - 27a. Caregiver 3-Month Follow-Up Assessment – for administration online
    - 27b. Caregiver 3-Month Follow-Up Assessment – for written administration
28. Caregiver 6-Month Follow-Up Assessment Version 1 – For Active Caregivers (ENGLISH VERSION)
    - 28a. Caregiver 6-Month Follow-Up Version 1 – for administration online
    - 28b. Caregiver 6-Month Follow-Up Version 1 – for written administration
29. Caregiver 6-Month Follow-up Assessment Version 2- For Bereaved Caregivers (ENGLISH VERSION)
    - 29a. Caregiver 6-Month Follow-Up Version 2 – for administration online
    - 29b. Caregiver 6-Month Follow-Up Version 2 – for written administration
30. Patient Baseline Assessment (SPANISH VERSION)
    - 30a. Patient Baseline Assessment - for administration online
    - 30b. Patient Baseline Assessment - for written administration
31. Patient Post-Decision Assessment Version 1 - Usual CEI Arm (SPANISH VERSION)
    - 31a. Patient Post-Decision Version 1 - for administration online
    - 31b. Patient Post-Decision Version 1 - for written administration
32. Patient Post-Decision Assessment - Investigational CEI Arm (SPANISH VERSION)
    - 32a. Patient Post-Decision Version 2 - for administration online
    - 32b. Patient Post-Decision Version 2 - for written administration
33. Patient 3-Month Follow-Up Assessment Version 1 - Usual CEI Arm (SPANISH VERSION)
    - 33a. Patient 3-Month Follow-Up Version 1 – for administration online
    - 33b. Patient 3-Month Follow-Up Version 1 – for written administration
34. Patient Follow-Up Assessment 1 - Investigational CEI Arm (SPANISH VERSION)
    - 34a. Patient 3-Month Follow-Up Version 2 – for administration online
    - 34b. Patient 3-Month Follow-Up Version 2 – for written administration
35. Patient Follow-Up Assessment 2 (SPANISH VERSION)
    - 35a. Patient 6-Month Follow-Up Assessment – for administration online
    - 35b. Patient 6-Month Follow-Up Assessment – for written administration
36. Caregiver Baseline Assessment (SPANISH VERSION)
    - 36a. Caregiver Baseline Assessment – for administration online
    - 36b. Caregiver Baseline Assessment – for written administration

37. Caregiver Follow-Up Assessment 1 (SPANISH VERSION)
    37a. Caregiver 3-Month Follow-Up Assessment – for administration online
    37b. Caregiver 3-Month Follow-Up Assessment – for written administration
38. Caregiver 6-Month Follow-Up Assessment Version 1 – For Active Caregivers (SPANISH VERSION)
    38a. Caregiver 6-Month Follow-Up Version 1 – for administration online
    38b. Caregiver 6-Month Follow-Up Version 1 – for written administration
39. Caregiver 6-Month Follow-Up Assessment Version 2 – For Bereaved Caregivers (SPANISH VERSION)
    39a. Caregiver 6-Month Follow-Up Version 2 – for administration online
    39b. Caregiver 6-Month Follow-Up Version 2 – for written administration

**Investigational Chemotherapy Educational Materials**

40. FOLFOX +/- bev CEI Materials (ENGLISH VERSION)
    a. Video & Website
    b. Booklet
41. FOLFIRI +/- bev CEI Materials (ENGLISH VERSION)
    a. Video & Website
    b. Booklet
42. FOLFIRINOX CEI Materials (ENGLISH VERSION)
    a. Video & Website
    b. Booklet
43. Gemcitabine + nab-paclitaxel CEI Materials (ENGLISH VERSION)
    a. Video & Website
    b. Booklet
44. Gemcitabine CEI Materials (ENGLISH VERSION)
    a. Video & Website
    b. Booklet
45. FOLFOX +/- bev CEI Materials (SPANISH VERSION)
    a. Video & Website
    b. Booklet
46. FOLFIRI +/- bev CEI Materials (SPANISH VERSION)
    a. Video & Website
    b. Booklet
47. FOLFIRINOX CEI Materials (SPANISH VERSION)
    a. Video & Website
    b. Booklet
48. Gemcitabine + nab-paclitaxel CEI Materials (SPANISH VERSION)
    a. Video & Website
    b. Booklet
49. Gemcitabine CEI Materials (SPANISH VERSION)
    a. Video & Website
    b. Booklet
50. Video Vignette – Coping with a new cancer diagnosis (ENGLISH & SPANISH VERSIONS)

51. Video Vignette – How do I feel the best that I can on chemo? (ENGLISH & SPANISH VERSIONS)