

Improving Informed Consent for Palliative Chemotherapy:  
RCT of Usual IC versus Investigational IC  
Dana-Farber IRB Protocol # 15-143

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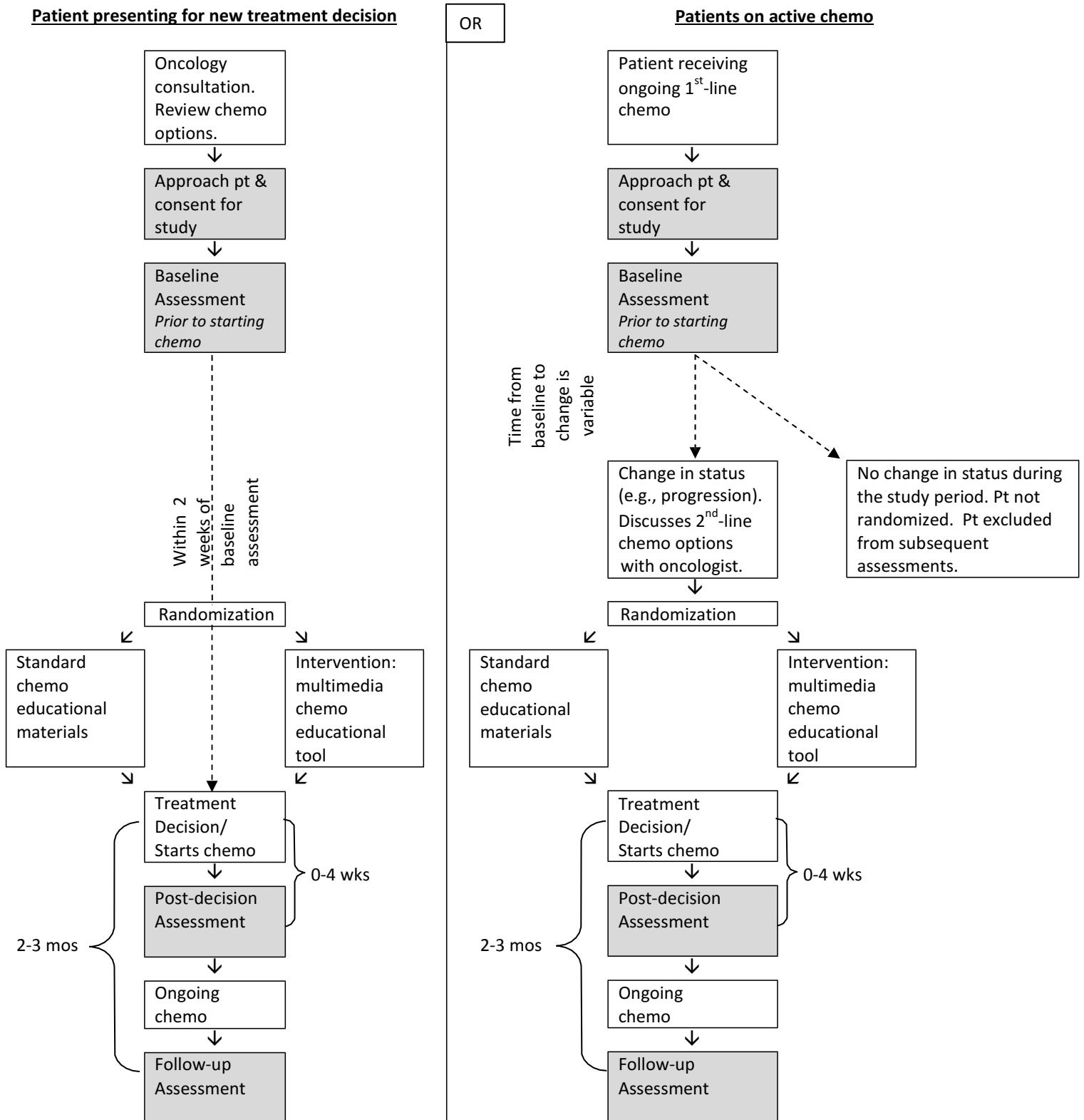
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## SECTION 1: Protocol Schema



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## SECTION 2: BODY OF PROTOCOL

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## 1.0 INTRODUCTION

### 1.1 Overview

Patients are routinely asked to sign an informed consent document prior to starting chemotherapy, indicating they understand the risks and benefits of treatment.<sup>1</sup> Although this could be a strategic moment to equip patients with information they need to make truly informed medical decisions, many patients and caregivers note that these conversations are less useful than they could be.<sup>1</sup> The informed consent process and its associated documents suffer several limitations: 1) risks are emphasized over benefits; 2) educational materials focus on individual drugs instead of regimens; 3) information is presented in written instead of alternative written/audiovisual format; and 4) the patient perspective is lacking.

Our research team, consisting of oncologists, nurses, and cancer patients has worked together to create a suite of informed consent tools which better convey the risks and benefits of common palliative chemotherapy options for advanced GI cancer. Each informed consent tool consists of a video 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 the patient perspective (e.g. video clips of patients describing their experience).

The overarching objective of this project is to conduct a randomized clinical trial to demonstrate if the informed consent toolkit the study team has developed improves the quality of informed consent for palliative chemotherapy. If effective, the tools will be amenable to broad dissemination via patient accessible cancer education websites and oncology clinics.

### 1.2 Background and Rationale

Choosing to pursue palliative chemotherapy is a complex decision for patients with incurable cancer. Patients must weigh the toxicities and benefits of chemotherapy in light of their priorities for what may be a very limited prognosis.<sup>1</sup> Over the past decade, it has become standard practice for oncologists to obtain informed consent (IC) from patients prior to initiating chemotherapy, whereby patients' attest they understand core information and agree to treatment.<sup>1,2</sup> The goal of IC is to equip patients with the knowledge to make an informed decision, including the purpose of treatment (e.g. cure versus palliate), benefits & risks, effects on prognosis & quality of life (QOL), and alternatives.<sup>1,2</sup>

The informed consent (IC) process for palliative chemotherapy is failing to achieve its purpose. Research indicates many patients lack the minimal understanding required for informed decision-making, particularly about the purpose and likely magnitude of benefits from palliative chemotherapy.<sup>3-5</sup> Although most patients indicate a preference for detailed information about their illness and an active role in their treatment decisions,<sup>6-8</sup> many harbor inaccurate and overly optimistic conceptions about potential benefits of palliative chemotherapy.<sup>4,5,9,10</sup> For example, they may think that treatment will cure their illness or extend their lives by many years, whereas several months is far more typical. We recently reported from the CANCORS<sup>9</sup> survey of 1193 cancer

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patients receiving palliative chemotherapy that 81% of colorectal cancer and 69% of lung cancer patients erroneously believed that chemotherapy might be curative.<sup>1</sup> These pervasive and fundamental misconceptions are concerning for several reasons. First, they call into question the validity and integrity of the current IC process. Second, inaccurate understanding of these issues impacts patients' end-of-life (EOL) medical care in troubling ways. Overly optimistic expectations of chemotherapy drive the use of late-line, minimally-effective chemotherapy,<sup>1,2</sup> and overoptimistic prognostic expectations are known to promote intensive and burdensome care near EOL.<sup>3</sup> Patients with metastatic colorectal cancer (mCRC) have a median survival of 2 to 2.5 years with therapy.<sup>1,2</sup> If such patients harbor false beliefs that chemotherapy may cure their cancer, they are robbed of opportunities to make the most of their remaining time, or plan for their care at EOL.

Widespread misunderstandings may relate to imperfect doctor-patient communication. Because patients look to oncologists for hope,<sup>3</sup> physicians may consciously or subconsciously magnify the benefits and suppress negative information about prognosis and the limitations of palliative chemotherapy.<sup>1-3</sup> Oncologists seek to establish therapeutic alliance with their patients, to convey hope, and to be well regarded by their patients. This may lead them to avoid explicitly discussing prognosis or survival benefits associated with chemotherapy, or to downplay potentially distressing information. For example: an analysis of audio-recorded oncologic consultations found that only 30% of visits included any discussion of the likelihood or magnitude of benefit associated with chemotherapy.<sup>1</sup> This directly conflicts with surveys demonstrating that the vast majority of patients want frank and complete disclosure, including quantitative information about treatment benefits.<sup>2-4</sup> Finally, even if the likelihood of benefit is discussed, many patients are overwhelmed at their initial consultation when these conversations typically occur, and may cling to the most optimistic scenarios and/or misinterpret the benefits of treatment.<sup>1,2</sup>

Chemotherapy informed consent (IC) documents do little to correct these misconceptions. Instead of providing balanced information about the risks and reasonably expected benefits of palliative chemotherapy, consent documents have become myopically focused on risk disclosure, resembling legalistic laundry lists of every possible toxicity.<sup>1</sup> Rather than viewing IC materials as helpful, most cancer patients perceive them to exist primarily as protection for physicians against litigation.<sup>1</sup> Other documents accompanying IC, such as chemotherapy information sheets, are similarly flawed by their technical language, risk emphasis, and focus on individual drugs. As a result, these documents do little to educate patients about the "big picture" of chemotherapy, and do not communicate clear information about risks/benefits/alternatives. Despite an overwhelming number of cancer related websites, information about prognosis and the magnitude of benefit from specific regimens is challenging to obtain.<sup>2</sup> Answers to questions such as, "what does this all mean for my future?" are exceedingly difficult to come by, which impedes patient-centered decision-making.

The optimal time to initiate frank conversations about prognosis and the likely benefits of palliative chemotherapy is at the outset of treatment.<sup>1,2</sup> At a new diagnosis of terminal cancer, patients may be overwhelmed and particularly prone to forming incorrect and overoptimistic beliefs about their illness. Correcting these mistaken beliefs after the fact is difficult because oncologists are usually unaware of their patients' misconceptions. Moreover, research suggests that early communication and understanding of prognostic and EOL issues may best support patients' ability to come to terms with their illness and make plans for care over the trajectory of their disease.<sup>2,3</sup> Evidence suggests that providing patients with tangible supplementary information about their illness and treatment,<sup>4,5</sup>

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and encouraging questions,<sup>6</sup> can improve patients' understanding of these topics without increasing distress. Because informed consent (IC) documents and chemotherapy information sheets are often distributed to patients, these tangible resources represent an attractive target for intervention,<sup>1,2</sup> which could be readily adopted within routine clinical practice. Conceptually, this strategy is also attractive because it may help provide extra support to oncologists as they convey difficult information about the limitations of palliative chemotherapy. We do not suggest that oncologists should (or want) to be absolved of the responsibility for conveying difficult information. However, access to high quality patient-centered educational materials may reinforce difficult information conveyed during oncology office visits, or fill in gaps that may have been omitted.

Advanced GI cancer represents an ideal model for augmenting chemotherapy informed consent (IC) tools. CRC is a major cause of morbidity/mortality, representing the third-leading cause of cancer related mortality among men and women in the US, with 50,310 people expected to die of CRC in the US this year.<sup>1</sup> The majority of mCRC patients undergo palliative chemotherapy; however, even with optimal treatment median survival is less than two years.<sup>2</sup>

Patients with mCRC have several treatment options, which differ in toxicity and in some cases efficacy.<sup>2,3</sup> These patients clearly face important decisions about their personal priorities in life, how to balance treatment intensity with quality of life, and planning for EOL care. For these reasons, mCRC represents an ideal paradigm in which to test the efficacy of multimedia IC tools, which if effective could be broadly applied to other cancer types.

**Intervention development:** Our research team has worked through a stakeholder-driven process to develop a suite of multi-media informed consent (IC) tools to support informed decision-making regarding palliative chemotherapy for advanced GI cancer. The suite includes five tools explaining: FOLFOX with or without bevacizumab and FOLFIRI with or without bevacizumab for mCRC as well as FOLFIRINOX, Gemcitabine, and Gemcitabine + nab-paclitaxel for advanced pancreatic cancer, which are recommended in national guidelines and represent the most common chemotherapy regimens used to treat these cancers.<sup>2,3</sup> Each informed consent tool is comprised of a video and a companion booklet, both of which are suited for review in clinic and to be taken home for patients and caregivers to review further. Each tool reviews core information important for an informed decision, including the purpose of treatment, its potential benefits, side effects, and alternatives. The tools also review logistics of treatment administration and contain optional information about prognosis.

Under Dana-Farber/Harvard Cancer Center IRB protocol #14-130, our intervention was evaluated by a panel of 56 patient advocates convened at the 2014 ASCO Annual Meeting, the vast majority (98%) of whom agreed that it would be useful to patients and promote informed decision-making. All advocates agreed that including patient voices was a key strength, and only 1 thought the tools would be too upsetting to patients. The intervention was also evaluated & highly rated by 25 expert GI oncologists representing 8 practices, all of whom reported that if they had access to these informed consent (IC) tools they would use them usually or always. Booklets and videos were revised according to patient advocate and oncologist feedback. Under Dana-Farber/Harvard Cancer Center IRB protocol #14-318, in-depth interviews were then conducted with metastatic colorectal cancer patients actively receiving palliative chemotherapy. Patients reviewed the intervention in detail and provided feedback and suggestion for improvement. Most suggestions were relatively minor (e.g. clarifying phrasing, re-filming a small section of film to improve eye-contact of the speaker). No adverse events occurred during the in-depth interviews. Thematic saturation was

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reached after 5 in-depth interviews. The IC tools were then revised according feedback from the in-depth interviews to create our final intervention.

## 2.0 OBJECTIVES

**Objective 1:** Determine if the multi-media informed consent (IC) tools improve patients' understanding of benefits and risks of palliative chemotherapy as compared to the standard IC process.

*Hypothesis:* The multi-media IC tools will decrease the likelihood that patients overestimate the curative potential of palliative chemotherapy as compared to the usual IC process.

*Hypothesis:* The multi-media IC tools will increase the likelihood that patients will have an accurate understanding of the risks of chemotherapy as compared to the usual IC process.

**Objective 2:** Determine if the multi-media informed consent (IC) tools enhance patients' prognostic understanding, increase advance care planning, and facilitate patient-physician conversations about end-of-life care preferences.

*Hypothesis:* Patients randomized to the intervention will have more realistic expectations of their prognosis as compared to patients randomized to the usual IC process.

*Hypothesis:* Patients randomized to intervention will be more likely to have designated a healthcare proxy and more likely to have a DNR order as compared to patients randomized to the usual IC process

*Hypothesis:* Patients randomized to the intervention will be more likely to discuss their end-of-life care preferences with their healthcare proxy, and with their oncologist as compared to patients randomized to the usual IC process.

## 3.0 RESEARCH SUBJECT SELECTION

### Eligibility Criteria

#### Inclusion criteria:

- Diagnosis of metastatic colorectal cancer **OR** locally advanced pancreatic cancer **OR** metastatic pancreatic cancer **AND**
  - Is making a decision regarding treatment with 1<sup>st</sup> or 2<sup>nd</sup> line palliative chemotherapy. **OR**
  - Is receiving 1<sup>st</sup> line palliative chemotherapy, and is therefore likely to make a future decision about 2<sup>nd</sup> line chemotherapy (either for cancer progression or toxicity). This cohort of patients will be eligible for study enrollment and baseline assessment, but will not be subject to randomization until the time of their next treatment decision.
- Treating oncologist has recommended consideration of one or more of the regimens for which we have developed informed consent (IC) toolkits (FOLFOX, FOLFOX + bevacizumab, FOLFIRI, FOLFIRI + bevacizumab, FOLFIRINOX, Gemcitabine, or Gemcitabine + nab-paclitaxel).
  - Patients who are also considering treatment on a clinical trial are eligible, including those considering treatment on a clinical trial of FOLFOX (+/-bev) + investigational agent, or FOLFIRI (+/-bev) + investigational agent
- Age  $\geq$  21
- English proficient

#### Exclusion criteria:

- Patients with oligometastatic disease to the lung and/or liver who are being treated with a definitive plan for curative surgical resection are not eligible.
- Significant delirium/dementia as judged by the treating oncologist

In addition, caregivers of eligible patients will also be eligible to participate in the caregivers assessments.

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**How caregiver participants will be defined, identified, and recruited:** In order to identify the appropriate caregiver, the research assistant will ask the consented patient who s/he would identify as his/her primary caregiver, if any. If the caregiver is physically present with the patient at the time the RA obtains the patient's consent, 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 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.**

#### 4.0 RESEARCH SUBJECT ENTRY

**Procedures for subject recruitment:** The research assistant will identify potentially eligible participants by looking through 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 potentially eligible participants.

- 1) For patients presenting to oncology clinic for an initial consultation/new treatment decision regarding first or second-line chemotherapy for their metastatic colorectal cancer, locally advanced pancreatic cancer, and metastatic pancreatic cancer: the research assistant will identify potentially eligible patients by screening new patient scheduling reports. The research assistant will notify the provider of the patients' potential eligibility prior to this initial consultation. Immediately after the consultation, the research assistant will contact the provider to confirm the patients' eligibility, and to 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.
- 2) For patients receiving ongoing first-line chemotherapy: The study research assistant will identify potentially eligible participants by screening existing patient scheduling reports, and accepting physician referrals. For potentially eligible patients, the research assistant will contact the treating oncologist or oncology nurse practitioner to ask permission to approach the patient for participation. Study research assistants will keep a log of the number of potentially eligible patients, the number of physician or nurse practitioner refusals, and the reason for those refusals.

**Procedure for research informed consent:** The research assistant will approach the eligible participant either in-person in the clinic, or over the phone and introduce the study, answer any questions, and offer the potential participant time to think it over. If/When the potential participant decides to participate, the research assistant will obtain signed informed consent for participation in the research study. The signed informed consent document will be returned to the study research assistant either in-person, via postal mail, or via email. If the potential participant decides NOT to participate, the study team will not contact the person again. The study research assistant will keep a log of the number of patient refusals, and the reason for those refusals. The caregiver will also be invited to participate; they will be given a study letter that contains the elements of informed consent.

**Procedure for registration:** After the participant signs written informed consent to participate in research,

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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 on page 2):**

1. For patients making a chemotherapy treatment decision at the time of study enrollment: After study consent and the baseline assessment, the study team will then randomize the patient to either the Usual IC Arm or the Investigational IC Arm of the study using REDCap's 1:1 randomization algorithm, stratified by 1<sup>st</sup>-line or 2<sup>nd</sup>-line chemotherapy.
2. For patients NOT making a new chemotherapy treatment decision at the time of study enrollment (e.g., they are receiving ongoing treatment with first-line palliative chemotherapy), randomization will occur at the point at which the patient is faced with a new chemotherapy treatment decision (e.g., for cancer progression, or treatment-related toxicity). Research assistants will contact the treating oncologists prior to scheduled chemotherapy visits and/or restaging visits to remind them of their patient's participation on the study, and to request that the oncologist contact the research assistant in the event that a new treatment decision is being made. When the patient's oncologist confirms that the patient is faced with a new chemotherapy treatment decision, the study team will then randomize the patient to either the Usual IC Arm or the Investigational IC Arm of the study using REDCap's 1:1 randomization algorithm, stratified by 1<sup>st</sup>-line or 2<sup>nd</sup>-line chemotherapy. Patients who do not make a new treatment decision during the timeframe of this study will not be randomized, and will not complete future study assessments.

Participants will be randomized 1:1 without blinding to receive either Usual Informed Consent or Investigational Informed Consent by utilizing a randomization algorithm managed by REDCap. This will be stratified according to whether the patient is 1<sup>st</sup> line palliative chemotherapy or 2<sup>nd</sup> line palliative chemotherapy.

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](mailto:Christine_cronin@dfci.harvard.edu), 617-632-3784.

When registering subjects, the study team will ask for the following information (see Appendix B):

- 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 genders
- Subject and caregiver's initials
- Subject and caregiver's ages
- Subject ID number
- Primary oncologist
- Confirmation of eligibility
- Stratification or classification factors (1<sup>st</sup> versus 2<sup>nd</sup> line palliative chemotherapy)

**Procedure for 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). The baseline assessment will be administered immediately after the participant signs informed consent; the baseline caregiver assessment will be administered immediately after the caregiver receives the

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study letter and agrees to participate. In rare cases when immediate administration is not possible, the central study research assistant at Dana-Farber will follow-up with the participant up to 3 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 3 attempts, then the study research assistant will mark the baseline assessment as missing and will not contact the participant about the baseline assessment again.

The post-decision assessment will be administered by the central study research assistant at Dana-Farber at any point between the day the participant starts chemotherapy and 4-weeks post-chemo start. During this 4 week period, the study research assistant will follow-up with the participant up to 3 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 3 attempts, then the study research assistant will mark the post-decision assessment as missing and will not contact the participant about the post-decision assessment again.

The follow-up assessment will be administered by the central study research assistant at Dana-Farber at any point between 2 months post-chemo start and 3 months post-chemo start. During this 1 month period, the study research assistant will follow-up with the participant and caregiver up to 3 times each. 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 3 attempts, then the study research assistant will mark the follow-up assessment as missing and will not contact the participant about the follow-up assessment again.

## 5.0 STUDY DESIGN AND METHODS

### 5.1 Design/Study Type

Non-treatment intervention, randomized clinical trial of up to 350 participants [244 patient participants plus up to 106 of their caregivers as caregiver participants] (social behavioral research).

### 5.2 Selection of Instruments

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.

Regardless of whether a participant is randomized to receive Usual IC materials or the Interventional IC materials, each participant will be asked complete three assessments:

#### **Instrument 1: Baseline Assessment (See Appendix C)**

The baseline assessment will assess socio-demographics, information/communication preferences, decision control preferences, and illness understanding. Patients will complete this assessment after consenting for the study, but before randomization. The baseline assessment takes approximately 5 minutes to complete.

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### **Instrument 2: Post-Decision Assessment (See Appendix E and Appendix F)**

Within 0-4 weeks of the participant's treatment decision, the participant will be asked to complete a post-decision survey assessing core understanding required for informed consent (IC) (risks, benefits, alternatives), understanding of illness (diagnosis, curability), decisional conflict, satisfaction with the IC materials, satisfaction with communication, and anxiety. The post-decision assessment takes approximately 20 minutes to complete.

### **Instrument 3: Follow-up Assessment (See Appendix G and Appendix I)**

Within 2-3 months of the participant's treatment decision, the participant will be asked to complete a follow-up survey assessing changes in treatment and illness understanding, decisional regret, communication satisfaction, care satisfaction & anxiety. The post-decision assessment takes approximately 20 minutes to complete.

**NOTE:** Participants will be asked questions about prognosis regardless of whether or not they skip the life expectancy sections in the booklet and video.

Immediately following completion of the follow up assessment: Using methods similar to those described by White et al<sup>11</sup>, the interviewer will show each participant his/her responses to the 2 questions about prognosis\*\*. Next, the interviewer will read the following standardized prompt: "Please take a moment to look at your responses. I notice that your answers to these two questions are [different/the same]. Can you tell me a little bit about this?"

The research assistant will then ask permission to audio-record the patient's answers. If the participant is willing to answer the question but declines audio-recording, notes will be taken during and after the interview. The RA will use standard cognitive interviewing techniques, such as reflexive listening, "think alouds" and standard probes ("can you tell me what you mean by that?") as necessary.

*\*\*Copy-pasted for reference - these are the 2 questions about prognosis:*

*Q: Based on what you have learned or been told, what is your understanding about how long the typical person with your type of cancer can expect to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

*Q: Every person is different and every situation is unique. If you had to make a guess - based on what you have learned about your cancer, your cancer treatment, and what you know about yourself - how long do you think that you have to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

**Medical Record Abstraction (see Appendix K):** Research assistants will perform medical record abstraction. 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 (Appendix K). See below for specific information

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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 (Appendix X).

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 Appendix X) 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 (Appendix K).

**Each caregiver will be asked complete two assessments:**

**Instrument 1: Caregiver Baseline Assessment (See Appendix D)**

The baseline assessment will assess socio-demographics, information/communication preferences, and illness understanding. The baseline assessment takes approximately 5 minutes to complete.

**Instrument 2: Caregiver Follow-up Assessment (See Appendix H and Appendix J)**

Within 2-3 months of the participant's treatment decision, the participant will be asked to complete a follow-up survey assessing changes in treatment and illness understanding, decisional regret, communication satisfaction, care satisfaction & anxiety. The post-decision assessment takes approximately 20 minutes to complete.

**CAREGIVER:** Immediately following completion of the caregiver follow up assessment, the interviewer will read the following standardized prompt:

How do you think the person for whom you care would answer this question? Could you tell me a little bit about why you answered in this way?

*Q: Based on what you have learned or been told, what is your understanding about how long the typical person with your type of cancer can expect to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

How do you think the person for whom you care would answer this question? Could you tell me a little bit about why you answered in this way?

*Q: Every person is different and every situation is unique. If you had to make a guess - based on what you have learned about your cancer, your cancer treatment, and what you know about yourself - how long do you think that you have to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5*

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*years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

The research assistant will ask permission to audio-record the caregiver's answers. If the participant is willing to answer the question but declines audio-recording, notes will be taken during and after the interview. The RA will use standard cognitive interviewing techniques, such as reflexive listening, "think alouds" and standard probes ("can you tell me what you mean by that?") as necessary.

**NOTE:** Caregivers will be asked questions about prognosis regardless of whether or not they skip the life expectancy sections in the booklet and video.

### 5.3 Description of Intervention

**Intervention Overview:** The intervention consists of 5 sets of chemotherapy informed consent (IC) tools. Each tool consists of a video and a complementary booklet which explain a common chemotherapy option for mCRC, locally advanced pancreatic cancer, or metastatic pancreatic cancer. This suite of tools reviews the following treatment options:

- IC Tool 1: FOLFOX & FOLFOX + bevacizumab are reviewed together in one IC tool, comprised of a video and complementary booklet
- IC Tool 2: FOLIRI & FOLFIRI + bevacizumab are reviewed together in one IC tool: comprised of a video and complementary booklet.
- IC Tool 3: FOLFIRINOX is reviewed in one IC tool: comprised of a video and complementary booklet.
- IC Tool 4: Gemcitabine + nab-paclitaxel is reviewed in one IC tool: comprised of a video and complementary booklet.
- IC Tool 5: Gemcitabine is reviewed in one IC tool: comprised of a video and complementary booklet.

➤ FOLFOX & FOLFOX + bevacizumab booklet – see Appendix N  
➤ FOLFOX & FOLFOX + bevacizumab video website – see Appendix O  
➤ FOLIRI & FOLFIRI + bevacizumab booklet – see Appendix P  
➤ FOLIRI & FOLFIRI + bevacizumab video website – see Appendix Q  
➤ FOLFIRINOX booklet – see Appendix R  
➤ FOLFIRINOX video website – see Appendix S  
➤ Gemcitabine + nab-paclitaxel booklet – see Appendix T  
➤ Gemcitabine + nab-paclitaxel video website – see Appendix U  
➤ Gemcitabine booklet – see Appendix V  
➤ Gemcitabine video website – see Appendix W

#### Description of informed consent (IC) videos

Each video is approximately 20 minutes and was filmed and edited by a professional health videographer. Videos and booklets are complementary but do not entirely overlap. DFCI 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.

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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. Videos will be accessible via a password-protected website suitable for viewing on tablet or computer.

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 informed consent (IC) booklets**

Booklets are regimen-specific IC documents, which serve as a regimen-specific educational tool and an acceptable documentation of IC. Content of the written IC tool adheres to regulatory requirements of IC with attention 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 is 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 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 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

### **Randomization and Administration of Intervention**

**Overview:** Patients randomized to the Usual IC Arm will undergo the standard institutional practice of informed consent for chemotherapy. At Dana-Farber, this will include receipt and signature of the standard institutional consent form for chemotherapy. The oncologist may also choose to give the patient the institutionally approved chemotherapy information sheets according to their preference (this is not a required practice at Dana-Farber).

### **Participating sites should follow their own institutional practices for usual informed consent.**

Patients randomized to Interventional IC Arm will be given regimen specific written and video Informed Consent tools developed by the study team. The treating oncologist will identify which chemotherapy regimen(s) are being considered, in order to select the appropriate informed consent (IC) tool(s) to give the patient. The patient may be given more than one IC tool if relevant; for example: if they are deciding between FOLFOX and FOLFIRI, they could be given both IC tools. Patients randomized to the intervention arm may receive the intervention in addition to OR in place of the

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standard institutionally approved chemotherapy information sheets (both are acceptable); this is at the discretion of the treating site or the treating physician. Patients randomized to the Interventional IC Arm will undergo informed consent for chemotherapy. This will include receipt of the investigational IC tool for chemotherapy in addition to OR in place of the standard institutionally approved chemotherapy teaching sheet.

At the beginning of the study period, the video and booklet informed consent tools will be shared with medical oncologists and nurse practitioners at a GI oncology staff meeting. The purpose of this orientation is to help facilitate any subsequent conversations about the study informed consent (IC) tools that might occur between providers and patients randomized to the intervention.

**Timing of intervention:** Patients randomized to the experimental arm of the study will be exposed to the intervention as soon as possible following the oncology visit discussing treatment recommendations (see protocol schema on page 1) and *prior* to their actual chemotherapy decision and treatment initiation. In select cases in which it is not possible to administer the intervention prior to their initiation of chemotherapy (e.g. such as a patient who opts to start a new chemotherapy regimen on the same day as their treatment discussion), it will be allowed to administer the intervention within 2 weeks of chemotherapy initiation. Every attempt will be made to ensure that the intervention is given to the patient as soon as feasibly possible, to ensure that the information is most relevant to them.

**Administration of intervention:** A research assistant or the treating physician/nurse practitioner (depending upon the preference of the physician/nurse practitioner) will give the patient the relevant informed consent (IC) booklet(s) along with printed information containing the URL address and password to the relevant IC video(s). The research assistant will offer to meet the patient in the clinic in order to orient them to the booklet and to allow them to watch the video on a study iPad. If the patient prefers not to review the study materials in clinic (e.g. due to inconvenience of scheduling), the study materials will be mailed to the patients' home, and the research assistant will follow-up by phone to answer any questions about accessing the video. Patients will be encouraged to review the booklet(s)/video(s) as many times as they wish, and will be encouraged to discuss any questions with their oncologist.

## 5.4 Data Collection

### Summary of measures used at each patient assessment

Domain	Measures	Baseline Assessment	Post-Decision Assessment	Follow-up Assessment
Socio-demographics <sup>a</sup>	Standard assessments	• x		
Health Literacy and numeracy <sup>b</sup>	Stagliano <sup>12</sup> (2013), Lipkus <sup>13</sup> (2001)	• x		
QOL <sup>c</sup>	FACT-G <sup>14</sup>	•	•	•
Optimism <sup>d</sup>	Life Orientation Test-Revised <sup>15</sup>	•		
Distress <sup>e</sup>	Emotional wellbeing component of FACT-G <sup>14</sup>	•	•	•
Communication & decision preferences <sup>f</sup>	Control Preferences Scale <sup>17</sup>	•		
	Preferred information for chemotherapy decision (for study)	• x		
	Prognostic communication preferences, Meropol <sup>16</sup>	• x		
Illness understanding	Developed for study	• x		
Use of IC booklet and video	Video use monitored via password protected website, booklet use monitored by survey		•	• x
<b>Quality of Informed Consent<sup>g</sup></b>				
Core Understanding				
Chemotherapy risks	Modified from Leighl et al <sup>18</sup>		•	
Chemotherapy benefits	Adapted from CANCORS <sup>9</sup> (primary outcome)		•	• x
Decision Making				

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Adequate information	Developed for study			
Decisional involvement	Modified Control Preferences Scale <sup>17</sup>		•	
Decisional conflict	Modified SURE assessment <sup>27</sup>		•	
<b>Satisfaction<sup>h</sup></b>				
MD-patient relationship	Revised Human Connection Scale <sup>19</sup>		• x	
With study IC tools/ standard IC	Developed for study		•	
With decision	Brehaut decisional regret scale <sup>20</sup>			•
<b>Doctor-patient communication<sup>i</sup></b>				
Patient-centered communication	Aurora and Mazor <sup>21</sup>		•	• x
Prognostic communication	Developed for study			• x
Prognostic Understanding <sup>j</sup>	Adapted from CANCORS <sup>9</sup>			• x
Advance Care Planning	Chart abstraction (DNR) and patient report (healthcare proxy)			• x

• Patient Participant Assessment

x Caregiver Participant Assessment

**Clinical characteristics:** Date of diagnosis (or metastatic recurrence), location of metastases, prior adjuvant chemotherapy, and ECOG performance status via chart review.

**<sup>a</sup>Socio-demographics:** Age, race/ethnicity, marital status, education, insurance status, preferred language, religious affiliation via chart review; and a one-item measure of religious coping via participant questionnaire.

**<sup>b</sup>Health Literacy & Numeracy:** Participants will complete a validated 1-item screening measure for health literacy developed by Stagliano,<sup>12</sup> and a validated 1-item screening measure to assess numeracy.<sup>13</sup>

**<sup>c</sup>QOL:** QOL will be assessed by the well validated Functional Assessment of Cancer Therapy-General (FACT-G)<sup>14</sup>, a 27-item scale assessing physical wellbeing, social/family wellbeing, functional wellbeing, emotional wellbeing, and functional wellbeing.

**<sup>d</sup>Optimism:** The validated 7-item Life Orientation Test-Revised<sup>15</sup> will assess trait optimism at baseline.

**<sup>e</sup>Distress:** will be measured using the emotional wellbeing subscale of the FACT-G QOL survey<sup>14</sup>.

**<sup>f</sup>Communication & decision-making preferences:**

Prognostic communication preferences: 5 items from an instrument developed by Meropol<sup>16</sup> et al will assess patients' preferences regarding prognostic communication (e.g. "I want to hear detailed statistics," "I want the doctor to speak to me in a positive manner") via participant questionnaire. Responses: "strongly agree," to "strongly disagree" on a 5-point scale.

Preferred information for chemotherapy decision: 7 items developed for the study will assess the amount of information patients want about each of the following topics relevant to chemotherapy informed consent: potential side effects, other treatment options, potential impact on quality of life, likelihood of cancer control, likelihood of cure, impact on length of life. Response options are on a 5-point Likert scale ranging from no information to as much information as possible.

Preferred involvement in care decisions: The Control Preferences Scale<sup>17</sup> is a validated 2-item measure of preferences for decision involvement (active, active-shared, collaborative, passive

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shared, or passive) via participant questionnaire.

### **Quality of Informed Consent:**

Understanding of chemotherapy benefits: The first primary outcome is a validated item from CANCORS.<sup>9</sup> Patients are asked: “After talking with your doctors about chemotherapy, how likely did you think it was that chemo would cure your cancer?” Responses (“very likely,” “somewhat likely,” “a little likely,” “not at all likely,” “don’t know”) will be dichotomized to accurate (“not at all likely”) and inaccurate (all others). The pre-specified time-point for assessing the primary outcome is at the follow-up assessment, although patients will also be asked this question at baseline and the post-decision survey. Similar to CanCORS<sup>9</sup>, patients will also be asked how likely they think it is that chemotherapy will “help you with problems or symptoms you are having because of your cancer,” “control the growth of your cancer,” and “help you live longer.” These additional items are included in the post-decision survey alone.

To assess understanding of treatment goal, patients are asked at the post-decision survey, “according to your doctor, what is the goal of the chemotherapy?” with the ability to choose any/all of the following response options: cure, control cancer growth, alleviate symptoms, prolong life, or other. Selecting either control cancer growth, and/or alleviate symptoms, and/or prolong life are defined as accurate understanding; “to cure” was inaccurate.

Understanding of chemotherapy risks: Modified items from Leighl et al<sup>18</sup> will assess patients’ understanding of the potential risks (e.g. side effects) of their chemotherapy choice via participant questionnaire. These items include understanding of key risks (e.g., FOLFOX+/-bevacizumab (e.g. fatigue, nausea/vomiting and neuropathy), and FOLFIRI+/-bevacizumab (e.g. fatigue, nausea/vomiting, diarrhea, hair loss)). The accuracy of patients’ understanding of chemotherapy risks will be scored based upon the chemotherapy regimen they opted to receive, as described below:

- Patients initiating FOLFOX or FOLFOX bev will be considered to have an accurate understanding of risks if they respond that they are somewhat/very likely to experience neuropathy and nausea and a little/not very likely to experience hair loss  
We will create similar algorithms for all of the other chemotherapy regimens based upon well-established toxicity profiles.

Adequate information for informed consent (IC): Patients will be asked whether they received the amount of information they desired regarding the following topics: potential side effects, management of side effects, potential impact on QOL, other treatment options, likelihood of cancer control, likelihood of cure, and potential impact on length of life, using a 5-point Likert scale from too far little information to far too much information.

Decisional Conflict & Decisional Control: Decisional conflict (representing potential conflict and satisfaction about a medical decision) will be assessed using a modified 6-item version of the SURE<sup>27</sup> assessment, which measures whether patients feel sure about what matters to them, understand their treatment options, understand the risks/benefits of those options, and feel supported in their decision.

Achievement of decisional control preferences (i.e. achievement of preferred role in treatment decision-

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making) will be assessed using the modified Control Preferences Scale (decisional involvement is compared with stated preferences).<sup>13</sup>

Decisional regret: Brehaut's validated 5-item scale will measure decision regret (scale 0-100).<sup>20</sup>

#### **hPatient Satisfaction**

**Satisfaction with informed consent (IC) materials:** Patients will rate their satisfaction with the IC documents (standard IC document and teaching sheets for patients randomized to UIC, or study IC documents). Patients randomized to investigational IC will also complete an assessment of the acceptability of the multimedia IC tool. Patients will self-report whether or not they read the booklet or watched the video, and how many times they reviewed it.

**Satisfaction with patient-MD relationship** will be assessed by 8-items from the Human Connection Scale<sup>19</sup>, which has been validated by its associations with patient quality of life, mood, and prospective association with end-of-life care patterns.<sup>10</sup>

**Satisfaction with the chemotherapy decision-making process** will be assessed via five items from the Patient Assessment of Cancer Communication Experiences<sup>22</sup> assessed in the post-decision survey (e.g. "I got clear, understandable information about the treatments we were considering," "I got consistent information from all my doctors and nurses; everyone was on the same page;" "My doctors and nurses helped me cope with the uncertainty or unknowns about my treatment decisions;" "I got a clear recommendation about what treatment approach would be best for me;" "I was encouraged to ask questions about my treatment choices;" "I felt my doctor understood what was important to me, and considered that in recommending a treatment"), with response options with 6 response options of never, sometimes, usually, always, or does not apply. Scores for these 6 items will be summed and averaged, creating a score of 1 to 4, with 4 being the most satisfied.

#### **iCommunication**

**Patient-Centered Communication:** the Patient Assessment of Cancer Communication Experiences developed by Mazor and Arora<sup>21</sup> will assess patients' perceptions of patient-centered communication at the time of 1) cancer treatment decision-making, and 2) chemotherapy treatment. At the post-decision assessment, 9 items will assess patient-centered communication regarding treatment decision-making. At the follow-up assessment, 11 different items will assess patient-centered communication while on active chemotherapy treatment.

**Prognostic communication:** At the follow-up assessment, patients will be surveyed regarding prognostic conversations they may have had with their oncologist, including whether their oncologist has discussed their life expectancy and who brought up the conversation.

**jPrognostic Understanding, care preferences and advance care planning:** Patients will be asked about their understanding of the typical life expectancy of patients' with their type of cancer. Using a single item adapted from CanCORS<sup>9</sup>, patients will be asked to estimate their own life expectancy.<sup>8</sup> They will also be asked about their preference for comfort-oriented versus intensive end-of-life care<sup>14</sup> using an item from SUPPORT. Patients will be asked whether they have designated a healthcare proxy, and whether they have discussed with their proxy their preferences for care should they become more seriously or terminally ill. Patients will also be asked whether they have discussed with their physician

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their preferences for care should they become more seriously ill, or terminally ill. Chart abstraction will determine whether the patient has completed a DNR order.

Participants will be asked questions about prognosis regardless of whether or not they skip the life expectancy sections in the booklet and video.

## 5.5 Description of Study Process

1. **IDENTIFY PARTICIPANTS:** The research assistant will identify potentially eligible participants by looking through 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 potentially eligible participants.
2. **CONSENT PARTICIPANTS:** The research assistant will approach the eligible participant either in-person or over the phone and introduce the study, answer any questions, and offer the potential participant time to think it over. If/When the potential participant decides to participate, the research assistant will obtain signed informed consent for participation in the research study. If the potential participant decides NOT to participate, the study team will not contact the person again. The caregiver will also be invited to participate; they will be given a study letter that contains the elements of informed consent.
3. **ADMINISTER BASELINE ASSESSMENT:** If the participant consents, the research assistant will administer the baseline assessment. For patients who are unable to complete the baseline assessment immediately following study consent (for example, if they are too fatigued or emotionally overwhelmed after their oncology consultation) the protocol will allow for participants to be randomized (see 4.0) and then complete the baseline survey (within two weeks of randomization). 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, 4) or by postal mail. Mode of collection will be recorded. The baseline assessment takes approximately 5 minutes to complete.
4. **RANDOMIZE PARTICIPANTS:** The research assistant will contact the central research assistant at Dana-Farber to randomize the participant:
  - A. For patients making a chemotherapy treatment decision at the time of study enrollment: After study consent and the baseline assessment, the study team will then randomize the patient to either the Usual IC Arm or the Investigational IC Arm of the study.
  - B. For patients NOT making a new chemotherapy treatment decision at the time of study enrollment (e.g. they are receiving ongoing treatment with first-line palliative chemotherapy), randomization will occur at the point at which the patient is faced with a new chemotherapy treatment decision (e.g. for cancer progression, or unacceptable treatment-related toxicity). After the patient's oncologist confirms that the patient is faced with a new chemotherapy treatment decision, the study team will then randomize the patient to either the Usual IC Arm or the Investigational IC Arm of the study.

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Participants will be randomized 1:1 without blinding to receive either Usual Informed Consent or Investigational Informed Consent by utilizing a randomization algorithm managed by REDCap. This will be stratified according to whether the patient is 1<sup>st</sup> line palliative chemotherapy or 2<sup>nd</sup> line palliative chemotherapy.

5. **ADMINISTER INTERVENTION:** For patients randomized to the intervention, the research assistant or the patient's oncologist or primary nurse practitioner (depending upon oncologist preference) will give the participant the relevant interventional informed consent (IC) materials.

The treating oncologist will identify which chemotherapy regimen(s) are being considered, in order to select the appropriate IC tool(s) to give the patient. Although we anticipate that most oncologists will recommend a single treatment option and will request that patients be given a single IC video and companion booklet, patients may be given both IC tools if the oncologist has recommended consideration of either FOLFOX(+/-bevacizumab), FOLFIRI(+/-bevacizumab), FOLFIRINOX, Gemcitabine + nab-paclitaxel, or Gemcitabine.

The patient will be given the investigational IC tools after discussing his or her treatment options with the oncologist, baseline assessment and randomization. Patients will be given the intervention IC materials *as soon as possible* after discussing treatment recommendations with their oncologist but *prior* to their actual treatment decision and initiation. In select cases in which it is not possible to administer the intervention prior to the initiation of chemotherapy (e.g. such as a patient who opts to start a new chemotherapy regimen on the same day as their treatment discussion), it will be allowed to administer the intervention within 2 weeks of chemotherapy initiation. Every attempt will be made to ensure that the intervention is given to the patient as soon as feasibly possible, to ensure that the information is most relevant to them.

Research assistants (or the oncologist, or NP if they choose to distribute the intervention) will give participants randomized to the intervention a hard copy of the relevant investigational IC booklet(s), and will show the participant the investigational IC video on a pre-loaded study iPad. Patients will be offered a private area to review the video (such as consultation room, or in private during their chemotherapy infusion). Caregivers will be allowed to join in the viewing, if the patient prefers. If the patient wishes to watch the video during their chemotherapy infusion but no private room is available (e.g. they are receiving treatment in a semi-private infusion area), they will use headphones so as not to expose other patients to the intervention. All participants will be given the URL address and password to take with them so that they will be able to access the video at any time, and will be given a copy of the booklet to take home. The website will have capability of tracking the frequency with which the video is viewed.

In rare cases when administering the intervention in person is not possible, the research assistant will send the participant the IC booklet (which will also contain the web address and password for the IC video) via postal mail or electronic mail. The study research assistant will call the patient within one week to answer any questions about how to access the video.

In cases in which the study research assistant gives the participant the investigational IC booklet and video, research assistants will make it clear that their sole purpose is to orient the patient to the booklet/video and answer questions regarding how to access the video website and/or use the study iPad to watch the video. If the participant asks the study research assistant any question

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about information presented in the investigational IC tools, the research assistant will refer the patient back to their primary oncologist, nurse practitioner, or infusion nurse.

6. **ADMINISTER POST-DECISION ASSESSMENT** within 0-4 weeks by the central research assistant at Dana-Farber after the day on which the participant made their treatment decision and initiated their new chemotherapy treatment. 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, 4) or by postal mail. Mode of collection will be recorded. The post-decision assessment takes approximately 20 minutes to complete.
7. **ADMINISTER FOLLOW-UP ASSESSMENT** within 2-3 months by the central research assistant at Dana-Farber after the day on which the participant made their treatment decision and initiated their new chemotherapy regimen. Questionnaire- based instruments will be administered to the participant and his/her caregiver 1) in person by a trained research assistant at the time of a routinely scheduled visit, 2) by e-survey, 3) by phone, 4) or by postal mail. Mode of collection will be recorded. The follow-up assessment takes approximately 20 minutes to complete.

**PATIENT:** Immediately following completion of the follow up assessment: Using methods similar to those described by White et al<sup>11</sup>, the interviewer will show each participant his/her responses to the 2 questions about prognosis\*\*. Next, the interviewer will read the following standardized prompt: “Please take a moment to look at your responses. I notice that your answers to these two questions are [different/the same]. Can you tell me a little bit about this?”

The research assistant will then ask permission to audio-record the patient’s answers. If the participant is willing to answer the question but declines audio-recording, notes will be taken during and after the interview. The RA will use standard cognitive interviewing techniques, such as reflexive listening, “think alouds” and standard probes (“can you tell me what you mean by that?”) as necessary.

*\*\*Copy-pasted for reference - these are the 2 questions about prognosis:*

*Q: Based on what you have learned or been told, what is your understanding about how long the typical person with your type of cancer can expect to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

*Q: Every person is different and every situation is unique. If you had to make a guess - based on what you have learned about your cancer, your cancer treatment, and what you know about yourself - how long do you think that you have to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

**CAREGIVER:** Immediately following completion of the caregiver follow up assessment, the interviewer will read the following standardized prompt:

How do you think the person for whom you care would answer this question? Could you tell me a

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little bit about why you answered in this way?

*Q: Based on what you have learned or been told, what is your understanding about how long the typical person with your type of cancer can expect to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

How do you think the person for whom you care would answer this question? Could you tell me a little bit about why you answered in this way?

*Q: Every person is different and every situation is unique. If you had to make a guess - based on what you have learned about your cancer, your cancer treatment, and what you know about yourself - how long do you think that you have to live?*

*A: 1, More than 10 years | 2, More than 5, but less than 10 years | 3, More than 3, but less than 5 years | 4, More than 2, but less than 3 years | 5, More than 1, but less than 2 years | 6, Less than 1 year*

The research assistant will ask permission to audio-record the caregiver's answers. If the participant is willing to answer the question but declines audio-recording, notes will be taken during and after the interview. The RA will use standard cognitive interviewing techniques, such as reflexive listening, "think alouds" and standard probes ("can you tell me what you mean by that?") as necessary.

Once the participant completes the follow-up assessment, the research assistant will inform the participant that his/her study participation is now complete and will remunerate him/her with a \$25 gift card (this applies to patient and caregiver participants).

In order to ensure that all interviews are being done correctly, all research assistants will undergo training in qualitative and cognitive interviewing from the SSMC (survey and stats methodology core). The study team investigators (Dr. Enzinger and Dr. Schrag) and a clinical social worker (Jane Bausch) will also conduct one-on-one training with all involved research assistants. This training will include a structural overview of the clinical teams involved with the care of GCC patients, and how to contact appropriate providers in a timely manner. Research assistants will be trained in how to recognize participant distress, assess its severity, and respond in an appropriate and compassionate manner. This training will include role plays modeling both mild, moderate and severe distress, with debriefing and feedback. The research assistant(s) will not implement this qualitative question until training in adverse reaction management has occurred.

The research assistant's first 3-5 cognitive interviews will be observed by a study investigator (Dr. Enzinger), who will offer post-interview debriefing and critiques. When RA has shown proficiency, RA would then conduct the qualitative interviews independently. A is the most appropriate person to conduct these interviews because patients/caregivers are already bringing up these issues exact within their interactions with her during the surveys.

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The study team will also ensure that all interviews are being done correctly by having the study team investigator (Dr. Enzinger) listen to a sample of interview audio recordings (2 randomly selected recordings per month for each research assistant conducting interviews). Weekly team meetings will also be held so that the study investigator and research assistants have an opportunity to discuss any questions or concerns arising during the previous week's interview process. During these team meetings, potential interview situations will be discussed and mock interviews may be conducted. In addition, study team investigators and researchers conducting the interviews will be in regular communication to ensure that interviews are being conducted on-time and in the appropriate way.

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## 5.6 Adverse Reaction and Their Management

Reporting adverse or unanticipated events: Investigators do not anticipate needing to remove a subject from the study for any adverse events. Subjects may decline to participate or withdraw their consent, as per standard policies and procedures. If a circumstance arose where the investigators were concerned about a subject's safety as a result of the study, the subject would be removed from the study. The proposed research will comply with the regulations set forth in CFR Part 46, Protection of Human Subjects. All staff involved in the proposed protocol have been educated regarding HIPAA regulations and fully understand their responsibility to safeguard the personal health information of every participant involved in the research.

Anticipated reactions: Adverse reactions are expected to be minimal. A possible adverse reaction as a result of participating in this study is psychological distress as a result of viewing the informed consent (IC) video and booklet, which discuss the fact that chemotherapy does not cure metastatic colorectal cancer. The IC booklet also includes an optional section that discusses typical life expectancy with and without chemotherapy. This optional section is sealed, and is preceded by a cautionary sign with explanation that normalizes patients' decision of whether or not to review it. The video similarly includes an optional web-link to a segment discussing life expectancy. This optional video web-link is also preceded by a cautionary explanation that normalizes patients' decision of whether or not to view this segment. Participants may also find some survey items regarding their prognostic understanding to be distressing; however we have worded these items carefully and with the input of patient stakeholders to ensure their sensitivity and acceptability to patients.

Reaction management: As explained above, our intervention is designed to minimize patient distress by making information about life expectancy completely optional and easy to avoid. Furthermore, patients will not be eligible for this study until after they have received an initial chemotherapy recommendation from their oncologist, a conversation which would have covered the fact that chemotherapy is not intended to cure metastatic colorectal cancer and may also have included conversation about prognosis. As mentioned above, sensitive aspects of the survey were carefully worded with the input of patient stakeholders to minimize potential for distress. Participants will be reminded that they may skip portions of the questionnaires that they find discomforting.

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.

The qualitative interviews, specifically, will include questions about prognosis. These questions are sensitive and may precipitate an emotional reaction for some patients. We propose the following plan should the patient exhibit mild, moderate, or severe distress during the interview.

- Mild distress: The research assistant will pause the interview, and ask the patient if they would prefer to skip the interview question or end the survey all together. The patient will be reminded that answering the qualitative question is entirely voluntary, and study participation is voluntary and can be ended at any time. At the end of the interview, or should the

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participant choose to end the interview, the research assistant will offer to contact a member of that patient's care team (nurse, social worker, primary nurse practitioner, or physician) to inform them of the event, or to speak with the patient in person (if the interview is taking place in clinic) or by phone.

- Moderate or severe distress: the research assistant will stop the interview, and immediately notify the patients' treating physician or nurse practitioner by page for immediate attention. They will also page the social worker on call for the DFCI GCC.

For any caregiver who exhibits severe distress as result of the study procedures, the study research assistant will notify the study PI, Dr. Deborah Schrag. Dr. Schrag will personally facilitate obtaining the appropriate support for the caregiver in distress, including possible mental health referral for the caregiver if necessary. Furthermore, caregivers will be reminded that participation is voluntary and can be stopped at any time for any reason.

All sites should notify the Overall PI, Deborah Schrag, MD, MPH, at [deb\\_schrag@dfci.harvard.edu](mailto:deb_schrag@dfci.harvard.edu) or 617-582-8301 within 24 hours of an adverse reaction. Dr. Schrag will notify the patient's primary oncologist and the Dana-Farber IRB, as appropriate. In concert with the primary oncologist, Dr. Schrag will ensure the patient received appropriate follow-up care.

## 5.7 Privacy and Confidentiality

### **Privacy Protections:**

Participants will be recruited and consented in-person in the clinic or via phone. The research assistant obtaining informed consent will ensure that these conversations occur in private or semi-private settings where others cannot overhear. If the participant signs consent, they will be given standard institutional Informed Consent materials which they can review silently (as these are paper documents) or the investigational IC materials (booklet and video) which they can review in private (if a private room is available) or in semi-private (in this case, we will ask the participant to watch the video using earphones to protect the patient's privacy).

Participants will be asked to complete 3 questionnaire-based assessments during the study period. If these are done in-clinic and if a private room is available, the research assistant may read the questions aloud to the participant and record the participant's answers, or the participant may complete the questionnaire silently using a study-provided iPad. If these are done via phone, the research assistant may read the questions aloud to the participant and record the participant's answers; the research assistant will conduct the phone questionnaire from a private location. In some instances, the central research assistant at Dana-Farber may email the REDCap questionnaire link to a participant; the participant will open the link, enter the survey using their unique study ID number, complete and submit the questionnaire online. The questionnaire will not request PHI and will be administered online using REDCap, a HIPAA-compliant, Partners'-managed electronic data capture platform.

Participant questionnaire responses will be recorded in a de-identified fashion using unique study ID numbers. The only key linking these unique study ID numbers to the participant's identity will be maintained by the study research assistant in a password-protected spreadsheet saved in a secure network folder. Hard-copy signed informed consent documents will be kept in the research assistant's locked drawer. At Dana-Farber, this is located at their Dana-Farber desk (Dana Bldg, 10<sup>th</sup> floor). Any hard-copy study documents will be kept in a study file in the research assistant's locked drawer

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separately from the signed informed consent documents.

Once the study is complete, the data collected will be aggregated and analyzed. All dissemination of results be aggregated and de-identified.

**Confidentiality Protections:**

The following information will be collected from or about study participants using unique study ID numbers (the only key linking these unique study ID numbers to the participant's identity will be maintained by the study research assistant in a password-protected spreadsheet saved in a secure network folder).

Medical record Abstraction: Baseline abstraction will collect date of diagnosis and stage at diagnosis, prior cancer surgeries, prior adjuvant or palliative chemotherapy and dates of administration, date of metastatic recurrence (if relevant), comorbid medical conditions, performance status. Post-decision abstraction will collect treatment decision made (e.g. what chemotherapy regimen, clinical trial, no chemotherapy). Follow-up abstraction will collect changes

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in treatment (e.g. dose reductions, change in chemotherapy), ER visits or hospitalizations, results of restaging scans (disease progression, stable disease, or response), and medical record documentation of advance care planning.

Questionnaire Administration: The baseline assessment will assess socio-demographics, information/communication preferences, decision control preferences, and illness understanding. Post-decision survey will assess core understanding required for informed consent (IC) (risks, benefits, alternatives), understanding of illness (diagnosis, curability), decisional conflict, satisfaction with the IC materials, satisfaction with communication, and anxiety. Follow-up survey will assess changes in treatment and illness understanding, decisional regret, communication satisfaction, care satisfaction & anxiety.

The raw data will only be shared with the study team at Dana-Farber Cancer Institute. Once the study is complete, the data collected will be aggregated and analyzed. All dissemination of results be aggregated and completely de-identified.

Data collected from this study will be retained for 5 years post study completion.

Hard-copy study materials will be kept in the research assistant's locked drawer. At Dana-Farber, this is located at their Dana-Farber desk (Dana Bldg, 10<sup>th</sup> floor). Electronic data will be kept in password-protected spreadsheets saved in a secure network folder accessible only to study team members and maintained by Dana-Farber IS. Data will be captured using REDCap, a HIPAA-compliant, Partners'-managed electronic data capture platform.

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## 6.0 STATISTICAL ANALYSIS

We will test hypotheses that the study intervention---informed consent (IC) video/written tools developed with patient and clinician input---can improve patient-centered decision making for subjects contemplating palliative chemotherapy for advanced GI cancer.

**Objective 1:** Determine if the multi-media informed consent (IC) tools improve patients' understanding of benefits and risks of palliative chemotherapy as compared to the standard IC process.

*Hypothesis:* The multi-media IC tools will decrease the likelihood that patients overestimate the curative potential of palliative chemotherapy as compared to the usual IC process. (primary study outcome)

*Hypothesis:* The multi-media IC tools will increase the likelihood that patients understand the goal of treatment as compared to the usual IC process.

*Hypothesis:* The multi-media IC tools will increase the likelihood that patients will have an accurate understanding of the risks of chemotherapy as compared to the usual IC process.

**Objective 2:** Determine if the multi-media informed consent (IC) tools decrease decisional conflict<sup>23</sup>, increase the likelihood patients achieve their preferred role in decision-making<sup>23</sup>, and increase satisfaction with the chemotherapy IC process as compared with the standard IC process<sup>22</sup>.

*Hypothesis:* The multi-media IC tools will decrease decisional conflict as compared to the usual IC process

*Hypothesis:* The multi-media IC tools will increase the likelihood that patients achieve their preferred role in treatment decision-making as compared to the usual IC process

*Hypothesis:* The multi-media IC tools will increase satisfaction with the chemotherapy IC process as compared to the usual IC process

**Objective 3:** Determine if the multi-media informed consent (IC) tools enhance patients' prognostic understanding, increase advance care planning, and facilitate patient-physician conversations about end-of-life care preferences.

*Hypothesis:* Patients randomized to the intervention will have more realistic expectations of their prognosis as compared to patients randomized to the usual IC process.

*Hypothesis:* Patients randomized to intervention will be more likely to have designated a healthcare proxy and more likely to have a DNR order as compared to patients randomized to the usual IC process

*Hypothesis:* Patients randomized to the intervention will be more likely to discuss their end-of-life care preferences with their healthcare proxy, and with their oncologist as compared to patients randomized to the usual IC process.

We will adhere to standard reporting principles delineated by the CONSORT statement for conduct and reporting of randomized trials. Primary reports will reflect the as randomized, "intention to treat" principle, however, we will also describe results according to actual exposure to the study interventions (based on patients' self-report of whether they reviewed the standard-of-care, or investigational chemotherapy informed consent materials). Fisher's exact test will test the difference between the study arms in the first primary outcome (the proportion of patients at follow-up assessment who fail to understand that chemotherapy is "not at all likely" to cure their cancer, as assessed by an item from CANCORS<sup>9</sup>). We will also test the influence of the intervention on secondary outcomes (e.g. understanding of the goal of palliative chemotherapy, chemotherapy risks, decisional conflict,

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achievement of preferred role in decision-making, satisfaction with chemotherapy IC process, prognostic understanding, advance care planning, discussion of end-of-life care preferences, satisfaction with MD communication, satisfaction with informed consent (IC) documents, decisional regret, emotional distress) using Fisher's exact or chi-square tests for dichotomous outcomes, and t-tests or Wilcoxon tests for linear outcomes. For missing data for primary or secondary outcomes, we will employ multiple imputation under a missing at random assumption<sup>24</sup>.

Subset analyses will explore the effect of the intervention on 1) patients making a decision about 1<sup>st</sup> line treatment, 2) patients making a decision about 2<sup>nd</sup> line treatment, 3) patients with colorectal cancer, and 4) patients with pancreatic cancer.

Because the effects of our intervention may be moderated by patient characteristics (e.g. age, race/ethnicity, health literacy and numeracy, communication preferences, decisional control preferences), we plan to conduct exploratory analyses investigating whether these factors moderate the effect of the intervention on outcomes including 1) accurate understanding of chemotherapy benefits, 2) satisfaction with communication and the IC tools, 3) decisional involvement, or 4) emotional distress. For example: we hypothesize that the IC tool may lead to decreased distress among patients who prefer a detail-oriented prognostic communication style, whereas it may lead to increased distress among patients who prefer a vague and support-focused prognostic communication style. We would also hypothesize that the effects of

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the intervention may be greater among patients with higher health literacy scores. We will test these hypotheses using multivariable logistic or linear regression analyses (depending upon the dependent variable), including interaction terms for collinear factors, and controlling for potential confounding factors (e.g. age, race/ethnicity, marital status).

**Power:** In the CANCORS<sup>9</sup> study, 80% of mCRC patients on 1<sup>st</sup> line chemotherapy thought that chemotherapy could potentially cure their disease (median of 4 months post-diagnosis). Based on previous series and projections about our patient mix, we anticipate that 60% of patients will have inaccurate expectations about the benefits of chemotherapy. If the intervention strategy is able to better align expectations with likely outcomes by one third (33%) we will deem the intervention as having major impact. If this benchmark 33% reduction is not achieved but the intervention exposed subjects nonetheless have expectations that are more accurate, we will view the intervention as beneficial but lacking major impact. Assuming a baseline 60% rate of inaccurate expectations about the benefits of chemotherapy, with a total of 194 patients, we will have 80% power to detect a 33% decrease (20% absolute decrease) in inaccurate expectations among patients exposed to the intervention with a one-sided type I error of 2.5%.

Open-ended comments in the patient and caregiver follow-up surveys regarding prognostic understanding will be transcribed verbatim with removal of all potential identifying information (e.g. names). The transcribed responses will then be analyzed using standard qualitative techniques. Borrowing from principles of grounded theory<sup>25,26</sup>, comments will be reviewed by two or more members of our research team until a set of themes emerges. Themes will be compared and revised in an iterative process with input from the lead study investigators as necessary to resolve differences. A coding manual will be developed using the final coding schema. Using this coding framework, each participant's response will be analyzed line-by line by two independent coders. Coders will be blinded to the participants' randomization group, although if the participant mentions the intervention within their response, this will not be stricken from the transcripts.

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## 8.0 APPENDICES A-X

### **Study forms and assessments:**

- Appendix A: Checklist for Participating Sites
- Appendix B: Registration Form
- Appendix C: Patient Baseline Assessment
- Appendix D: Caregiver Baseline Assessment
- Appendix E: Patient Post-decision Assessment – Usual IC Arm
- Appendix F: Patient Post-decision Assessment – Investigational IC Arm
- Appendix G: Patient Follow-up Assessment – Usual IC Arm
- Appendix H: Caregiver Follow-up Assessment – Usual IC Arm
- Appendix I: Patient Follow-up Assessment – Investigational IC Arm
- Appendix J: Caregiver Follow-up Assessment – Investigational IC Arm
- Appendix K: Medical Record Abstraction Form
  
- Appendix L: Phone script for approaching potential participants via phone
- Appendix M: Phone script for assessment administration

### **Investigational IC Arm:**

- Appendix N: FOLFOX+/-bevacizumab booklet
- Appendix O: FOLFOX+/-bevacizumab video website
- Appendix P: FOLFIRI+/-bevacizumab booklet
- Appendix Q: FOLFIRI+/-bevacizumab video website
- Appendix R: FOLFIRINOX booklet
- Appendix S: FOLFIRINOX video website
- Appendix T: Gemcitabine + nab-paclitaxel booklet
- Appendix U: Gemcitabine + nab-paclitaxel video website
- Appendix V: Gemcitabine booklet
- Appendix W: Gemcitabine video website
  
- Appendix X: Global Medical Record Release Form
  
- Appendix Y: Study Letter for Caregiver Participants